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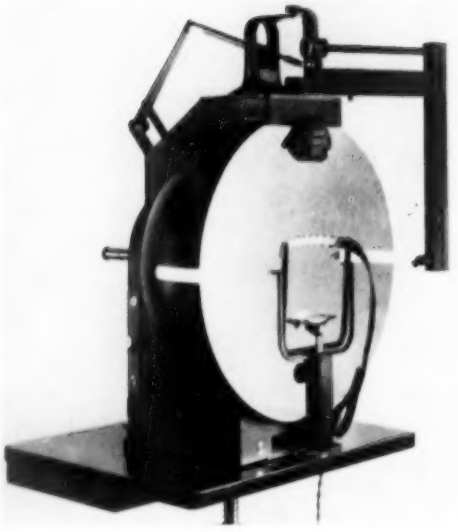

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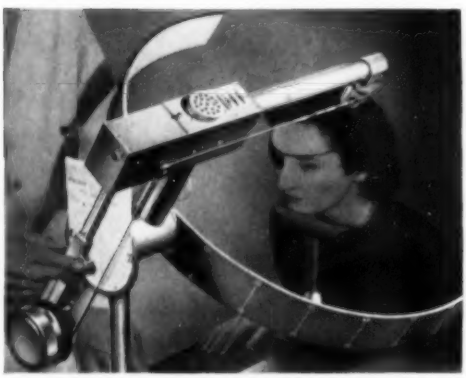

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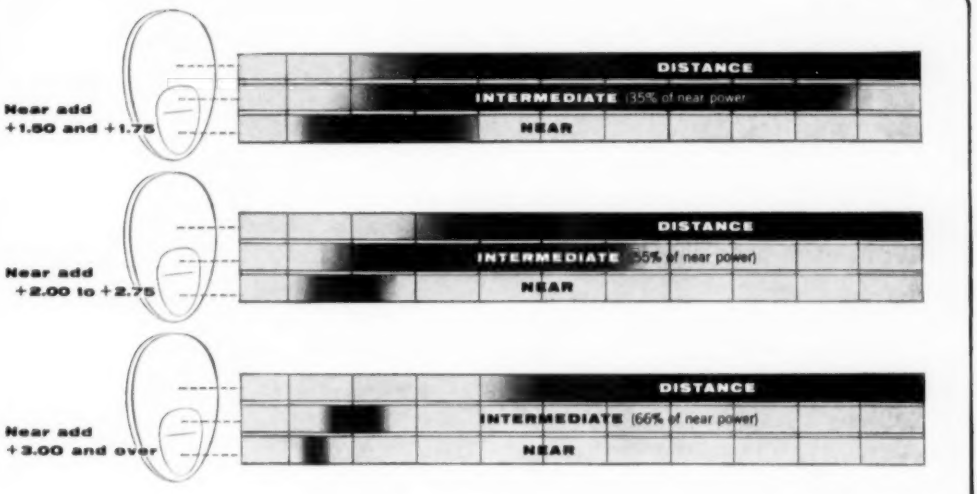

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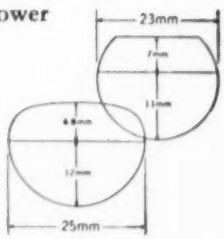

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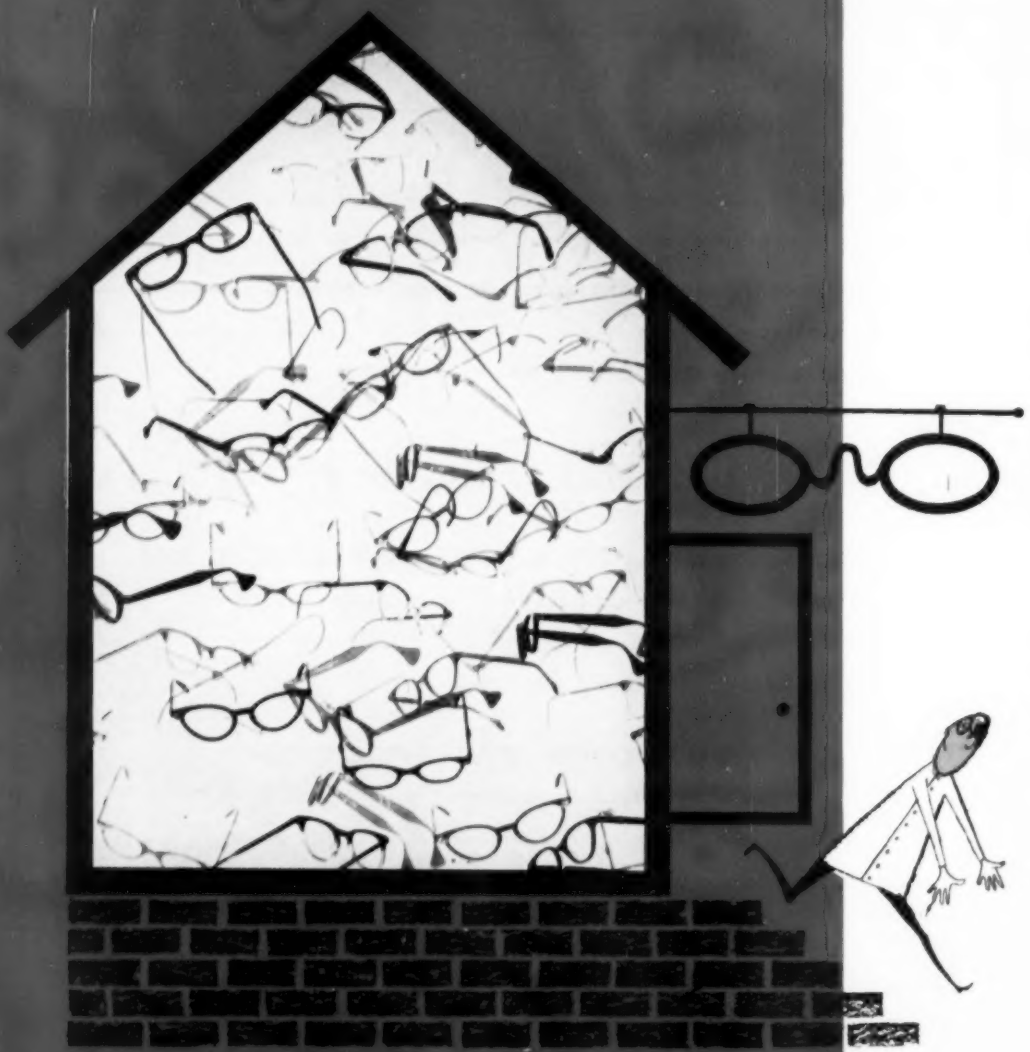

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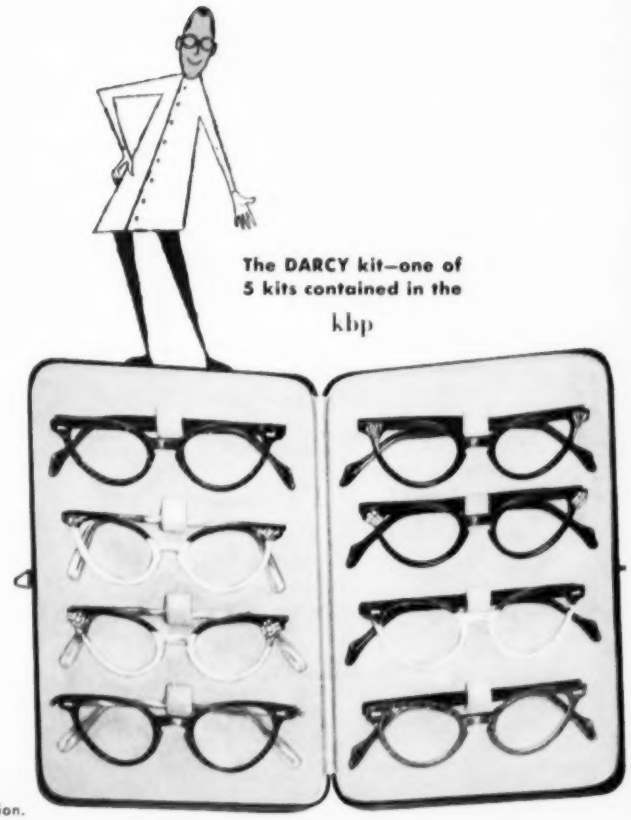

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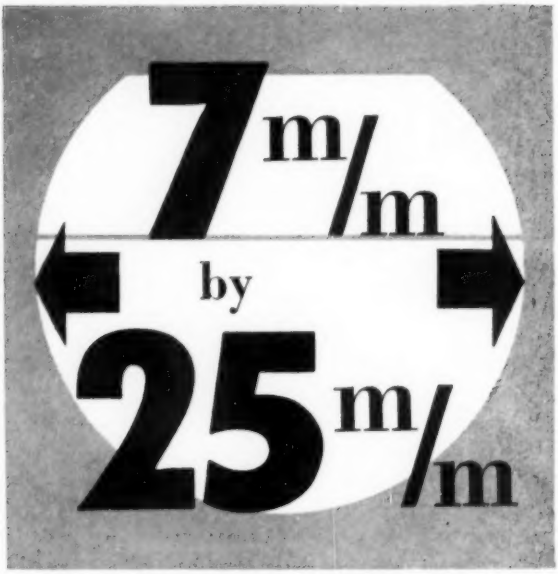

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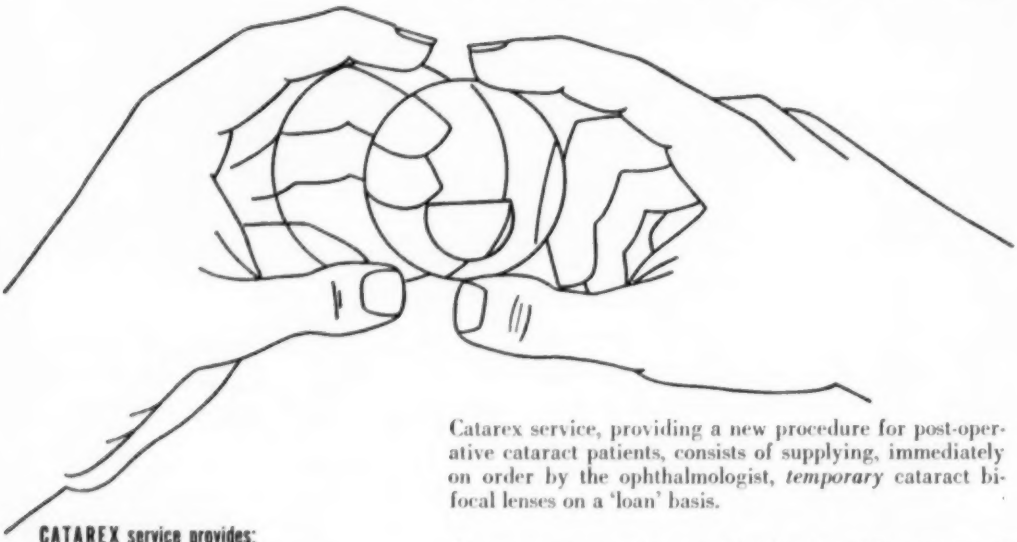

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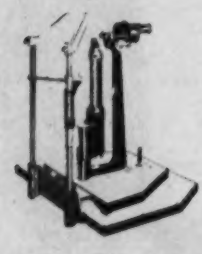

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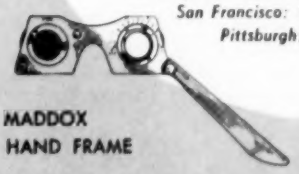

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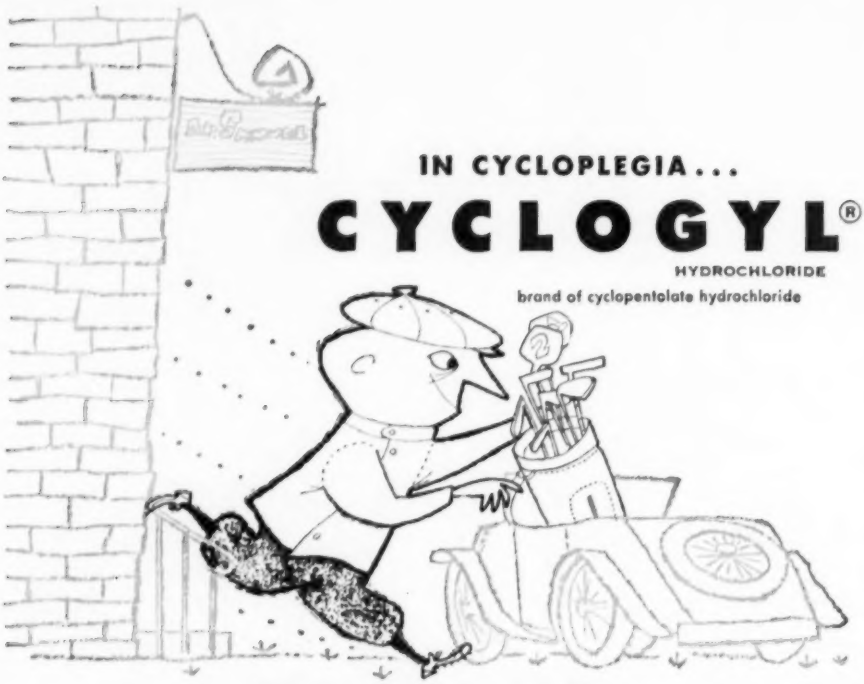

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1. Gordon, D. M., and Ehrenberg, M. H.: Am. J. Ophth. 38:831 (Dec.) 1954.

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Angle-Closure Glaucoma

Subacute Types

PAUL A. CHANDLER, M.D.
and
ROBERT R. TROTTER, M.D., Boston

It is now generally accepted that there are two fundamentally different types of primary glaucoma, the so-called wide-angle (open-angle) and the narrow-angle (angle-closure) glaucoma. While the two types have in common an obstruction to outflow of aqueous from the anterior chamber, and hence an elevated ocular tension, which results in loss of function of the eye, there is a fundamental difference in the two types in respect to the mechanism of the obstruction to outflow. In wide-angle glaucoma (hereinafter referred to as open-angle glaucoma), aqueous has access to the filtration apparatus at all times, and the obstruction to outflow of aqueous resides in the filtration apparatus itself (corneoscleral meshwork, Schlemm's canal, aqueous veins). In narrow-angle glaucoma (hereinafter referred to as angle-closure glaucoma), the filtration apparatus is at first normal, and obstruction to outflow is due solely to closure of the angle by contact between the iris root and the trabecular wall, and hence prevention of access of aqueous to the filtration apparatus. At a later stage, after repeated episodes of angle closure, there may be damage to the corneoscleral meshwork.

One might represent diagrammatically the difference between the two types.

From the Howe Laboratory of Ophthalmology, Harvard Medical School, and Massachusetts Eye and Ear Infirmary.

This study was supported by Research Grant B-218 of the Institute of Neurological Diseases and Blindness of the National Institutes of Health, U. S. Public Health Service.

Figure 1 represents a chamber angle of normal width, everywhere open, with no pathology visible by gonioscopy and with free access of aqueous to the filtration area. Such a picture is seen with the goniolens in both the normal eye and the eye with primary open-angle glaucoma. Figure 1, Inset *A*, shows the angle cross section in a normal eye whose aqueous flows out at a normal rate, maintaining normal intraocular pressure, with very small diurnal fluctuation; the filtration apparatus is normal. Figure 1, Inset *B* is identical except that the question mark suggests some abnormality in the filtration apparatus which offers increased resistance to the escape of aqueous humor and causes elevation of ocular tension. This is the situation in primary open-angle glaucoma, in which the tension varies from time to time in relation to changes in resistance to aqueous outflow, and probably to changes in rate of aqueous formation as well. Such variations in ocular tension may be as small as 10 to 15 mm. Hg during a 24-hour period in the average untreated case of open-angle glaucoma, or as great as 30 to 50 mm. Hg, especially in younger patients.

Figure 2 pictures the chamber angle in a glaucomatous eye with some iris convexity, shallowing of the anterior chamber, and a somewhat narrower angle than is shown in Figure 1. Such an angle remains open at all times, whether the tension is normal or elevated. Obstruction to outflow of aqueous (Fig. 2, inset) is due, just as in the wide-angle type, to some abnormality of the filtration apparatus. Thus, a shallow anterior chamber and narrow angle in the presence of elevated tension does not automatically make the diagnosis angle-closure glaucoma.

Figure 3 represents the situation in early angle-closure glaucoma during a phase of normal tension; the angle is narrow but open. Figure 3, Inset *A* shows a flat iris with

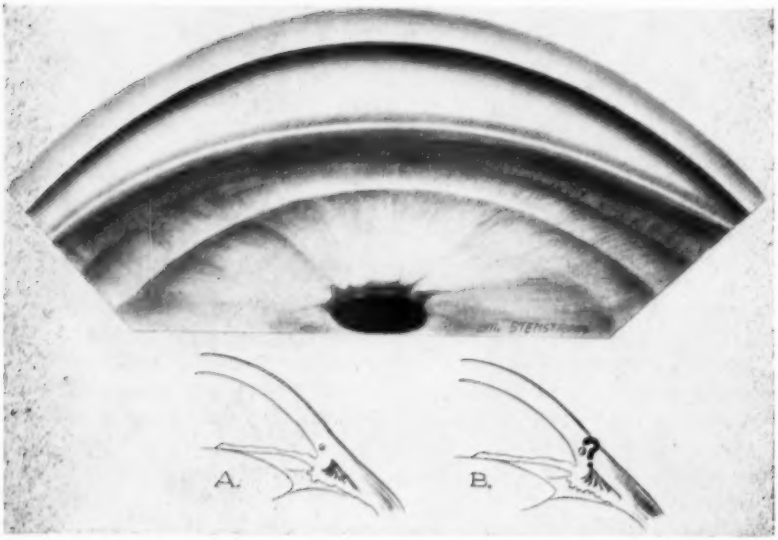
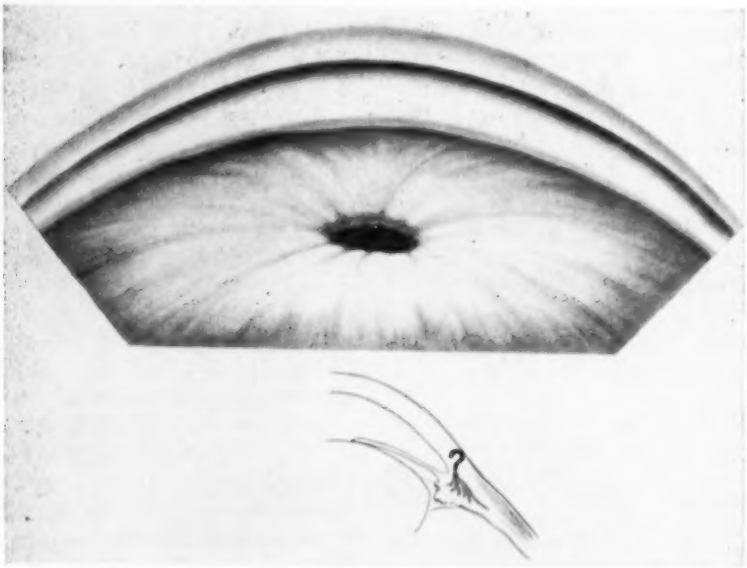


Fig. 1.—Open angle (wide): Angle structures are all readily seen by gonioscopy; iris plane is flat, and aqueous has access to filtration apparatus at all times. Inset *A*: Cross section of such an angle in a normal eye; the filtration apparatus is unimpaired. Inset *B*: Cross section of such an angle in an eye with open-angle glaucoma. Question mark suggests abnormal filtration apparatus, with reduced aqueous outflow and tension rise as a consequence of the abnormality.

Fig. 2.—Less roomy angle in eye with open-angle glaucoma: Iris is more convex, anterior chamber shallower over-all, and the angle narrower than in the more frequently seen (wide) configuration illustrated in Figure 1. This angle would not close on pupillary dilatation. Inset: Cross section of angle with question mark again suggesting abnormality of filtration apparatus.



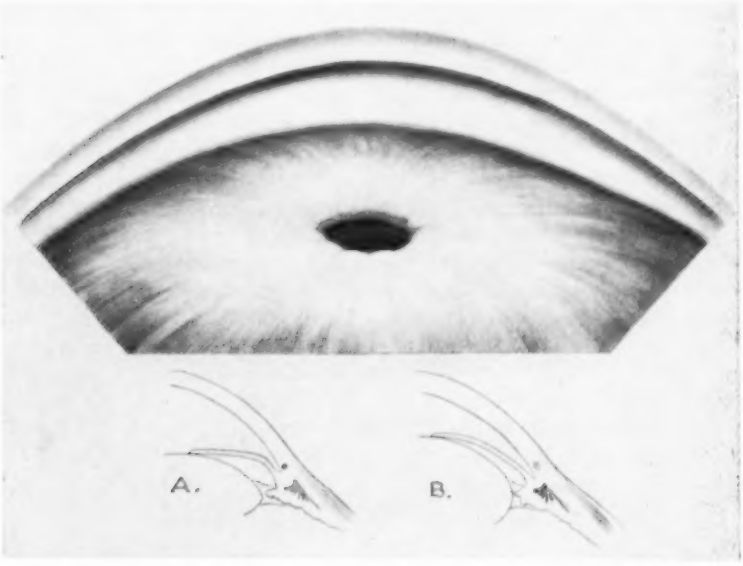


Fig. 3.—Chamber angle in early angle-closure glaucoma: During a phase of normal tension the angle is narrow but everywhere open; aqueous has access to the normal filtration apparatus, and tension is normal. Inset *A*: Iris is rather flat axially, but the convex iris periphery creates narrowness of the angle. Inset *B*: Cross section of the more usual narrow angle with over-all iris convexity, pictured in the large view above.

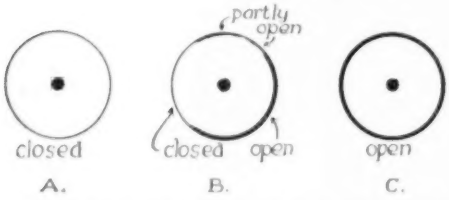


Fig. 4.—Degrees of closure seen in angle-closure glaucoma: Complete, as seen in an attack of acute angle closure with high tension (*A*); partial, with varying widths, in an attack of subacute angle closure with tension less high than in the acute form (*B*); angle altogether open and tension normal (C).

peripheral convexity. Figure 3, Inset *B* shows the more usual configuration of over-all iris convexity. In such eyes the tension is normal at all times as long as the angle is open, because aqueous has access to the filtration apparatus, which, as pictured, is normal and offers no obstruction to outflow. Only minor fluctuations in tension occur during the 24-hour period as long as the angle stays open, just as in the completely normal eye. Such eyes are, in fact, normal during this period; glaucoma does not exist at the moment; it is potential.

Figure 4 indicates schematically the degrees of closure which may occur in an eye with narrow angle of the type susceptible to closure: complete (or nearly so) in an attack of acute angle-closure glaucoma (Fig. 4*A*); partial, in an attack of subacute angle-closure glaucoma (Fig. 4*B*); no closure, during periods of normal tension (Fig. 4*C*). When the angle closes, although the filtration apparatus is still normal, aqueous cannot get to it because the iris is in contact with the trabecular wall; thus, aqueous cannot escape, and tension rises. When the angle is entirely closed, or nearly so, in a typical attack of acute angle-closure glaucoma (Fig. 4*A*), the tension becomes very high.

Figure 5 (and Fig. 4*B*) show, however, that in a typical attack of subacute angle-closure glaucoma only part of the angle is closed at one time, and tension therefore does not rise to the levels seen in the acute form of the disease.

The purpose of this paper is to point out the characteristics of the subacute types of angle-closure glaucoma and to discuss the rationale of treatment in clinical cases. Subacute angle-closure glaucoma may be defined as a form of glaucoma in which the elevation of tension is due solely to closure of the angle, but in which the entire angle is not closed at one time, so that the attacks of elevated tension are not as severe and intractable as in acute glaucoma. In the early stages the eye returns completely to normal between attacks. After repeated attacks a portion or portions of the angle may remain closed by peripheral anterior synechias, or the trabecular meshwork may be damaged by the repeated closures of the angle, or both may occur.

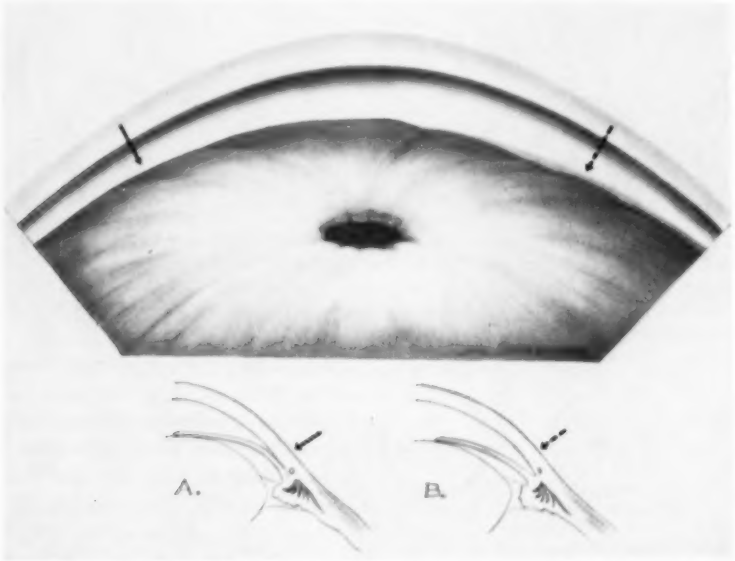


Fig. 5.—Angle during an attack of subacute angle-closure glaucoma: Access of aqueous to the normal filtration apparatus is blocked in some areas (solid arrow) by apposition of iris and trabecular wall, preventing escape of aqueous. In unclosed areas (broken arrow) aqueous can reach the filtration channels and escape from the eye. The tension level is somewhat proportional to the circumferential extent of blockade.

REVIEW OF LITERATURE

There is very little in the literature dealing specifically with subacute angle-closure glaucoma. The "chronic congestive" glaucoma in von Graefe's original classification and in most classifications since his time probably refers to subacute angle-closure glaucoma. Ophthalmology is indebted to Barkan for the first classification of primary glaucoma based on the gonioscopic appearance of the chamber angle. He divided primary glaucoma into two great types, trabecular (open-angle) and iris block (angle-closure) glaucoma. Barkan recognized the subacute types as an entity and recommended peripheral iridectomy (multiple or single) for the early cases and a filtering operation for the more advanced.* Curran [4] in 1920 reported cases which from his description appear to be of the subacute angle-closure type, in which the glaucoma was apparently relieved by peripheral iridectomy or iridotomy.

Goldman,[5] in 1947, classified glaucoma as glaucoma simplex, acute glaucoma, and chronic congestive glaucoma. He noted that in glaucoma simplex the angle remained open during a period of elevated tension. In acute glaucoma he found the angle closed when tension was elevated. There was no

* References 1, 2, and 3.

cupping of the disc. In chronic congestive glaucoma he stated that during a phase of elevated tension a portion of the angle was closed. Glaucomatous excavation of the disc was apparent. He noted that in chronic congestive glaucoma the "outflow pressure" was normal during a phase of normal tension. In other cases, especially with elevated tension, he found varying degrees of increase in outflow pressure. He concluded that variations in outflow pressure were apparently due to various degrees of angle closure.

Grant [12] has pointed out that in the subacute types of angle-closure glaucoma there is close correlation between closure of the angle, as observed gonioscopically, and the height of the tension and facility of aqueous outflow. He noted that in the subacute types the glaucoma was bilateral much more frequently than in the acute form.

Miller [6] gave a beautiful clinical picture of subacute angle-closure glaucoma in terms of symptomatology and tension studies, based on the observation of 100 cases. He pointed out the association of attacks of elevated tension with attendance at movies, reading in dim light, and exposure to dim light. He observed that as the disease progresses the attacks of elevated tension come more frequently, the base pressure rises, and cupping and atrophy develop. He gave no gonioscopic findings and did not discuss treatment. One of us (P. A. C.),[7] in a general discussion of narrow-angle (angle-closure) glaucoma, gave a brief discussion of the diagnosis and treatment of the subacute types.

CHARACTERISTICS OF SUBACUTE ANGLE-CLOSURE GLAUCOMA

I. *The Chamber Angle.*—The angle is anatomically narrow. Under the influence of various physiologic factors, which have been discussed elsewhere,† such as relative pupillary block, dilatation of the pupil, marked constriction of the pupil (in rare cases), and sudden dilatation of the uveal vessels, a portion of the angle closes and tension rises to a varying degree. Either spontaneously or under the influence of miotics, the angle again opens completely, and tension returns to normal. During the course of repeated episodes of angle closure, especially if they continue for some time, the iris in some places becomes permanently attached to the trabecular wall (peripheral anterior synechias). Under the influence of miotics or spontaneously, the remainder of the angle opens and the tension falls. If only a small portion of the angle remains permanently closed by peripheral anterior synechias, tension returns completely to normal. If a considerable portion remains closed, tension cannot be brought fully to normal by miotics, but can be only more or less reduced. There is hence a rise in "base pressure." [11] If a large portion of the angle is permanently closed, tension remains permanently elevated in spite of all treatment with miotics. There is a marked variation in the tendency of eyes to form peripheral anterior synechias. In some eyes, in spite of repeated and long-continued closure of the angle, adhesions do not form, and the angle still opens completely under miotic treatment. In other eyes, peripheral anterior synechias apparently form very readily, so that even early in the course of the disease extensive peripheral anterior synechias may develop. Even in eyes in which peripheral anterior synechias do not form, if the disease is advanced, tension cannot be fully normalized with miotics and outflow is impaired. It would appear that repeated episodes of angle closure finally cause permanent damage to the corneoscleral meshwork. This will be discussed more fully below.

II. *Clinical Picture.*—1. History: In most cases there is a history of periodic attacks characterized by more or less ocular discomfort, blurred vision, and seeing colored haloes around lights. The attacks are commoner during the winter than during the summer months (possible influence of light on the pupil). They are commoner during the late afternoon and evening than during the morning (possible influence of lighting and fatigue). They are often precipitated by emo-

† References 1, 4, 8, 9, 7, 10, and 15.

tional upsets (possible influence of pupillary dilatation or congestion of uveal vessels), especially by watching moving pictures and television and driving at night (possible influence of pupillary dilatation). The frequency of attacks varies in different patients. They may occur daily or at intervals of several days or weeks. Miller [8] reported a case in which 19 attacks occurred during a period of three months.

2. External Examination: The eye is usually white and quiet, or nearly so. The anterior chamber is usually rather shallow over-all, but in some cases may be only slightly shallow axially, and fairly shallow in the periphery. The cornea may be clear or may show more or less epithelial edema, depending on the height of the tension. As the slit-lamp beam is moved out toward the periphery of the cornea, the iris is seen to come closer and closer to the cornea, until in the extreme periphery it almost, or quite, touches the cornea. The pupil is usually slightly dilated if tension is elevated. It reacts normally if tension is normal at the time of examination, more or less sluggishly if tension is elevated.

3. Ophthalmoscopic Examination: The disc may be completely normal or may show more or less cupping and atrophy, depending on the stage of the disease. If disc changes are present, there is characteristically a predominance of atrophy, with less cupping evident than is usually seen at a comparable stage of open-angle glaucoma.

4. Tension: Tension may be normal if taken between attacks, or may show varying degrees of elevation. Except in the most advanced cases tension is seldom found higher than 50 to 60 mm. (Schiøtz) during an attack.

5. Gonioscopy: Gonioscopic examination shows, as a rule, a marked convexity of the iris, sometimes of the entire iris, sometimes chiefly the peripheral portion. In some cases, however, as noted by Barkan,[10] the plane of the iris is relatively flat. This is more commonly observed in eyes with a normal, or only slightly shallow, axial depth of the anterior chamber. If the tension is normal, the angle, though narrow, may be everywhere open, or a small portion may be closed. As a rule there is a considerable variation in the width of the angle. One may observe cases in which in one area, usually nasally, the angle is of good average width, and one can readily see the scleral spur and ciliary band, whereas in all other areas in the same eye the angle is extremely narrow and one cannot even make out the scleral spur. If gonioscopy is done when the tension is elevated, one sees a varying extent of the angle closed. The upper portion of the angle is usually the first to close; the nasal portion, the last. When the disease is advanced, more or less of the angle may be permanently closed by peripheral anterior synechias. When gonioscopic examination is done during a period of elevated tension and a portion of the angle is seen to be closed, one cannot tell whether the closure represents simple contact or permanent peripheral anterior synechias. This can only be determined by reexamination after the tension in the eye has been reduced medically or surgically. One sees some eyes in which it is very difficult to determine gonioscopically whether the angle is closed or there is a slit-like space between the iris and the trabecular wall.

In a case of known glaucoma with a shallow anterior chamber, if gonioscopy is done when the tension has been brought to normal or near-normal with miotics, one may find the angle on gonioscopic examination to be narrow, but everywhere open. One cannot tell at this point whether the case is one of open-angle or of angle-closure glaucoma. Miotics are then discontinued and tension allowed to rise. Gonioscopic examination is then done again while the tension is elevated. If the angle remains open with tension elevated, the diagnosis must be open-angle glaucoma. If, on the other hand, a portion of the angle is found to be closed when the tension is elevated, the diagnosis is angle-closure glaucoma.

6. Perimetry: The field may be normal or show more or less glaucomatous defects, depending on the degree of cupping and atro-

phy of the disc. Since atrophy is usually a more prominent feature than cupping, field defects are often surprisingly large, considering the appearance of the disc.

7. Tonography: Grant [12] has made many outflow studies in the subacute types. He states:

> In the subacute and chronic forms of narrow-angle glaucoma the same sort of mechanism appears to exist, in that obstruction to aqueous outflow measured tonographically can be satisfactorily correlated with the tension and with the degree of closure of the angle. In the subacute and chronic forms the degree of obstruction to outflow was found to be moderate in comparison with that in acute narrow-angle glaucoma. Outflow appeared to be obstructed functionally and reversibly in some instances by forward bulging of the periphery of the iris, but in most eyes there was also some degree of permanent obstruction by peripheral synechias. In some eyes only by intensive use of miotics could the facility of aqueous outflow and the tension be improved to normal medically, but relief of the obstruction due to forward bulging of the iris was generally aided by iridectomy. After iridectomy the angle was seen to become wider, as it did in treatment of the acute form, and the outflow of aqueous was found to be facilitated to the extent permitted by residual peripheral anterior synechias.

8. Provocative Tests: When in a given patient the anterior chamber is observed to be shallow and the history is suggestive of attacks of glaucoma, certain provocative tests may be of assistance in establishing the diagnosis, though a negative provocative test does not completely rule out the possibility of glaucoma.

(*a*) Moving picture test. The patient is sent to a movie matinee and reports within 15 or 20 minutes to the oculist's office. This test has proved to be of considerable value.

(*b*) Darkroom test.[12] The patient spends one hour in a darkroom or with the eyes bandaged so as to exclude light. The patient must remain awake. Tension is measured before and after this period. A rise of 8 mm. Hg (Schiøtz) or more is generally considered significant.

(*c*) Mydriasis test. Dilatation of the pupil with a weak mydriatic may bring about a rise in tension. It is questionable whether this test should be widely employed, since in the beginning one cannot be sure whether one is dealing with a potential acute or a potential subacute case, and dilatation of the pupil with drops may precipitate an acute irreversible attack.

(*d*) Reading in dim light. As pointed out by Miller,[8] prolonged reading in dim light may in certain predisposed eyes cause a sharp rise in tension.

MEDICAL TREATMENT

Medical treatment consists in the use of the usual miotics. The strength and frequency of administration of the drugs are judged by their effects on the tension. The goal is the complete prevention of periodic rises of tension. Every important rise in tension is due to closure of some portion of the angle; and the longer the duration of the closure, the greater the possibility that it may be made permanent by persisting peripheral anterior synechias. Medical treatment, therefore, must be considered to be inadequate if it permits any significant rise of tension, even though such elevation does not persist long enough to cause permanent loss of function.

SURGICAL TREATMENT

For the early cases we believe that any significant rise in tension under faithful miotic treatment justifies surgical intervention, and the operation of choice, as in early acute glaucoma, is peripheral iridectomy. Filtering operations designed to increase drainage from the anterior chamber would appear to be illogical and unjustified in a case in which, when the angle is open, the facility of aqueous outflow is normal. Peripheral iridectomy, as has been pointed out by others,‡ relieves the relative pupillary block, widens the chamber angle, and prevents future closure. If the operation is done before the corneoscleral meshwork has been damaged by repeated angle closure, and before the angle is permanently obstructed by peripheral anterior synechias, iridectomy apparently effects a complete and permanent cure of the glaucoma, and no further treatment is necessary.

‡ References 1, 4, 7, 8, 9, 10, and 15.

If the disease is moderately advanced, but tension can be normalized with miotics, peripheral iridectomy will eliminate any periodic acute rise in tension, but may leave a certain amount of permanent residual glaucoma, owing to a damaged corneoscleral meshwork or peripheral anterior synechias, which can often be controlled by the continued use of antiglaucoma drugs. After peripheral iridectomy, epinephrine bitartrate, phenylephrine hydrochloride, and miotics, including isofluorophate (diisopropylfluorphosphate), can be used when needed as safely as in open-angle glaucoma.

If the glaucoma is already far advanced when treatment is begun, a large portion of the angle is usually permanently closed by peripheral anterior synechias, tension cannot be lowered with miotics, and peripheral iridectomy is of no avail. For such cases a filtering operation is required, and iridencleisis with or without sclerectomy is the recommended operation.

How can one judge in the individual case whether peripheral iridectomy with or without the continued use of antiglaucoma drugs will be sufficient to control the disease? The response to miotic treatment is a valuable guide here. If the tension can be brought to normal or near-normal with reasonable use of miotics,§ and gonioscopic examination shows a large portion of the angle free of peripheral anterior synechias, peripheral iridectomy is the operation of choice, even though there are marked cupping and atrophy of the disc and marked field changes. On the other hand, if the tension remains considerably elevated in spite of regular miotic treatment, and gonioscopic examination suggests extensive peripheral anterior synechias, a filtering operation should be chosen. In borderline cases we believe peripheral iridectomy should be tried first. It can be done in the 10:30 or 1:30 o'clock position, and if the residual tension is still too high, an external filtering operation or cyclodialysis can be done later.

As far as we are aware, filtering operations, particularly iridencleisis, have heretofore been commonly employed for the subacute types of angle-closure glaucoma, irrespective of the stage of the disease. The glaucoma, to be sure, has been arrested in a good percentage of cases by this procedure. In fact, in many instances the glaucoma has been relieved by a filtering operation when there was no evidence of filtration whatever. These eyes have had, in effect, an iridectomy by the roundabout route of an unsuccessful filtering operation.

TECHNIQUE OF PERIPHERAL IRIDECTOMY

A technique for peripheral iridectomy has been described in detail by one of us (P. A. C.).[7] We believe this to be the simplest and safest method for the average ophthalmologist. Points that deserve emphasis are that the incision should be started 2 mm. outside the limbus, it should be beveled toward the angle of the anterior chamber, it should be only long enough to admit small iris forceps, and it should be tightly closed with a deep scleral suture. Either a limbus- or fornix-based conjunctival flap may be employed. If the iris cannot be made to prolapse, it is always advisable to sweep the wound with an iris repositor to make sure all peripheral anterior synechias are freed before introducing iris forceps. If this is not done, it may be difficult to introduce iris forceps into the anterior chamber without tearing the iris, or possibly injuring the lens.

Of course, a keratome or small knife could be used for the incision. Except in the most skillful hands, there is some risk with the keratome of injuring the lens, on the one hand, or of splitting the cornea, on the other. The knife incision, for technical reasons, must be longer than necessary, is usually not sufficiently beveled, and hence is more difficult to close tightly. One cannot overemphasize the importance of tight closure of the wound to obviate any possible chance of a flat anterior chamber after operation. We have seen eyes lost as a direct result of a flat anterior chamber from leakage of the wound after peripheral iridectomy. If the operation is to be employed as a prophylactic procedure for certain fellow eyes with beginning glaucoma, as we believe it should, the surgical technique must be faultless.

§ By reasonable use of miotics is meant use of the ordinary miotics every three or four hours. It should be emphasized that normalization of tension by intensive use of miotics does not necessarily mean that the angle has opened largely or completely, and hence cannot serve as a guide in the choice of operation.

POSTOPERATIVE COURSE AND TREATMENT

At the conclusion of the operation an antibiotic ointment is instilled and only the eye operated on is bandaged. The following day the pupil is dilated with 10% phenylephrine hydrochloride, and is dilated daily thereafter until the eye is quiet. If there is evidence of postoperative iritis and the pupil does not dilate well, homatropine, scopolamine, atropine, and cortisone are used as indicated.

In some cases in which the tension cannot be brought to normal or near-normal preoperatively with miotics and the tension is fairly high at the moment of operation, one may find a considerable elevation of tension in the immediate postoperative period. A tension of 40 to 50 mm. has been observed on several occasions, and in one eye the tension was 70 mm. Hg (Schiøtz) on the third postoperative day.

Although it has not yet been confirmed by gonioscopic examination, we believe this rise in tension in the immediate postoperative period is probably due to closure of the angle from swelling of ciliary body and iris. It is, therefore, a matter of some concern, since permanent closure of a portion of the angle could ensue from peripheral anterior synechias. The usual miotics plus epinephrine bitartrate 1% should be used as indicated. The tension usually falls to normal in a matter of hours or days, and the strength and frequency of miotic treatment are gradually reduced. In the earlier and more favorable cases no miotics are used postoperatively, the angle is gonioscopically open, and it would appear that the glaucoma is completely and permanently cured.

Malignant glaucoma ‖ may follow operative intervention in certain cases of subacute angle-closure glaucoma if the tension is considerably elevated at the time of operation, irrespective of the type of operation employed. One should make every effort, therefore, with miotics and every other medical means, to bring the tension to normal, or as near normal as possible, preoperatively. Only in this way can a malignant postoperative course be prevented in predisposed eyes.

‖ By malignant glaucoma is meant a form of postoperative ocular hypertension in which the anterior chamber never re-forms and the tension steadily rises.

COMMENT

The physiologic abnormality in eyes with subacute angle-closure glaucoma consists in periodic closure of a portion of the angle under the influence of such factors as dilatation of the pupil, reading in dim light, and emotional upsets. This angle closure brings about an elevation of ocular tension in proportion to the extent of the angle which closes. If this periodic closure of the angle can be prevented by medical or surgical means, the glaucoma is completely arrested. Tonographic measurements in the intervals between attacks of elevated tension have repeatedly shown a normal facility of aqueous outflow in the early cases. From a theoretical standpoint, therefore, there is no justification for filtering operations in such cases. If outflow facility is already normal, provided the angle can be kept open, there would appear to be no logic in attempting surgically to make it greater than normal. Peripheral iridectomy or iridotomy in the early cases (if there are no peripheral anterior synechias) should theoretically, by relieving relative pupillary block, prevent closure of the angle. A considerable experience with clinical cases attests to the fact that this operation does afford complete protection against future attacks of angle closure, and hence a permanent cure of the glaucoma. Barkan [8] has reported a similar favorable experience. Filtering operations for the early cases are therefore unnecessary from both a theoretical and a practical standpoint and are attended by a far greater surgical risk than peripheral iridectomy. Delayed re-formation of the anterior chamber is not uncommon after filtering operations. In predisposed eyes it may result in permanent closure of a considerable portion of the angle by peripheral anterior synechias, and if a good filtering scar does not develop, the glaucoma may be made considerably worse by the operative intervention. Other undesirable consequences of delayed re-formation of the anterior chamber are

complete posterior synechias with inflammatory pupillary membranes, since the pupil cannot be dilated while the anterior chamber is flat, and opacities in the lens. Even in cases in which there was no possible trauma to the lens during operation, prolonged contact between cornea and anterior lens capsule may result in anterior capsular and subcapsular opacities, which may progress to a degree causing serious impairment of vision. Furthermore, the cornea in certain predisposed eyes may be permanently edematous as a result of long-delayed re-formation of the anterior chamber.

In more advanced cases with extensive peripheral anterior synechias, where tension cannot be materially reduced by miotics, it is obvious that outflow facility of aqueous must be markedly reduced, filtering operations would appear necessary from a theoretical standpoint, and practical experience reveals that they are, in fact, necessary to provide normalization of tension.

There remains a group of cases in which the glaucoma is moderately advanced or advanced, as evidenced by changes in the disc and the visual field, yet which show few, if any, peripheral anterior synechias, and the angle opens completely, or nearly so, under the influence of miotics. The tension, however, may not come fully to normal in spite of the open angle, and outflow facility may be more or less impaired. We have assumed that in these cases repeated episodes of angle closure have brought about permanent changes in the corneoscleral meshwork. Verhoeff,[14] in 1912, presented histologic evidence that in certain cases sclerosis of the corneoscleral meshwork was caused by peripheral anterior synechias which have become freed. We find that in his Case 8 the clinical history, although meager, indicated a subacute angle-closure glaucoma as the original condition.

Clinical History. The patient, a man aged 67, has had no vision in the left eye for fifteen years. Three years ago he began to have attacks of redness and pain. Six weeks ago he began to have pain in the right eye and to see colored rings around lights. Vision of the right eye was 20/30; field considerably contracted. The left eye was enucleated April 16, 1910.

Pathologic Condition. There were advanced primary glaucoma, deep cupping of the optic disc and advanced atrophy of the retina and iris. The ciliary body was moderately atrophic. The pupil was free. The filtration angle was everywhere free, except as noted below. The ligamentum pectinatum in places was covered with a layer of vascularized hyaline tissue, sometimes containing elastic tissue and presenting a smooth surface lined by endothelium. In other places the spaces of Fontana were partly opened and the surface of the ligament was ragged, showing portions of iris tissue adherent to it. Here, the opposite surface of the iris was also ragged. In one place the angle was bridged by a strand of iris tissue containing a blood vessel. The spaces of Fontana were for the most part obliterated, and the trabeculae were not easily recognized.

Thus, Verhoeff found marked changes in the corneoscleral meshwork and undoubted evidence that at least a portion of the angle had been previously closed. Barkan[8] has recently called attention to the possibility of damage to the corneoscleral meshwork from repeated episodes of angle closure. He observed a pigment band on the trabecular wall, which he assumed had been left there during a period of angle closure. In one such case the residual glaucoma after peripheral iridectomy was relieved by trabeculotomy.

In these moderately advanced and advanced cases, in which the angle opens largely or entirely under miotic treatment, if tension can be normalized by miotics, peripheral iridectomy is justified as the initial operation. It will prevent future episodes of angle closure, and the residual glaucoma, presumably due to a damaged corneoscleral meshwork, can usually be controlled by medical means. If, however, in such cases tension cannot be reduced to normal or near normal by miotics, even though the angle largely or completely opens, a filtering operation is indicated.

The possibility of the formation of peripheral anterior synechias, or permanent damage to the corneoscleral meshwork as a result of repeated episodes of angle closure, provides strong justification for early operation, before such irreversible changes have taken place in the angle.

In nearly all cases of subacute angle-closure glaucoma in one eye, the fellow eye is affected sooner or later. We have advocated and employed prophylactic peripheral iridectomy for such fellow eyes except in aged, debilitated, or chronically ill patients. The risk of such operation, if properly performed, is minimal. Without operation many such eyes are eventually lost through neglect on the part of the patient or physician. It is, unfortunately, not common to effect a permanent and complete cure of glaucoma, but peripheral iridectomy for early subacute angle-closure glaucoma, as in early acute glaucoma, apparently does effect such a cure, and there is no aspect of the entire glaucoma problem which provides such satisfaction to both patient and ophthalmologist.

REPORT OF CASES

CASE 1.—A woman aged 30 was first examined in April, 1952, when she complained of pain in both eyes, with blurring and haloes. Uncorrected vision was 6/6—3 in the right eye and 6/6 in the left, and tensions measured 22 and 14 mm. Hg (Schiøtz) in the right and left eyes, respectively. Corneas were 12 mm. in diameter. The right pupil measured 3 mm., and the left 3.5 mm., and both were readily reactive. Anterior chambers were of normal depth. Optic nerve heads and visual fields were normal.

Later that day, tensions were measured at 32 mm. in the right eye and 21 mm. in the left, and tonography (without miotics) showed markedly impaired outflow in the right eye and normal outflow in the left eye. Gonioscopy showed the irises to be fairly flat; the chamber angles were very narrow bilaterally, and were functionally open in the left eye but partially closed in the right eye. Light thrown into the pupil opened the angles. A tentative diagnosis of bilateral intermittent angle-closure glaucoma was made, and the patient was placed on miotic therapy.

Three months later, normal tensions having been measured at intervening visits, the patient saw haloes all evening after attending a movie. A few days later peripheral iridectomy was done bilaterally. During the first six weeks after operation tensions in the left eye remained in the 'teens, while in the right eye they were measured in the high 20's. Three months after surgery the patient admitted having attacks of blurred vision, right eye, lasting for about an hour, accompanied by slight aching but no haloes. Examination showed both eyes to be white and quiet, and no miotics were given.

Two years after operation, the uncorrected vision was 6/21 (pinhole 6/7.5) in the right eye and 6/9 in the left. The patient admitted experiencing occasional pains (probably) in the left eye, of some minutes' duration, and not accompanied by blurring or haloes. Examination showed the anterior chambers to be of average depth, the lenses clear, the discs normal. Pupils were equal in size and brisk in reaction. Tension was 21 mm. in each eye, and facility of aqueous outflow was equal and normal in both eyes. Gonioscopy showed the iris to be flat, and the peripheral iris billow to be separated from the trabeculum by a narrow slit in both eyes, except for a somewhat wider area in the temporal angle of the left eye. The presence or absence of peripheral anterior synechias could not be told with certainty, but widening of the angles was distinctly less than that seen postoperatively in the more usual case, which shows greater iris convexity before operation.

CASE 2.—A man aged 66 was first examined Feb. 20, 1951, complaining of a blur in the right eye the previous week. (Tension had been measured at 40 mm. Hg [Schiøtz] by the referring physician.) Examination showed corrected vision of 6/12 in the right eye and 6/9 in the left eye. Tensions were 32 mm. Hg (Schiøtz) right and 19 mm. left, with miotics. The anterior chambers were very shallow; the pupils were 3 mm., the right pupil reacting only slightly. The right nerve head showed shallow glaucomatous cupping, and the visual field revealed a lower Bjerrum scotoma, as well as nasal contraction; the left disc was normal, as was the field.

Two weeks later, after 18 hours without drops, tensions were measured at 52 mm. in the right eye and 20 mm. in the left eye. The pupils measured 3 mm. and were reactive. Facility of aqueous outflow was markedly impaired in the right eye and was normal in the left eye. Gonioscopy showed the irises to be only slightly convex. The filtration area was blocked by iris in the right eye; the meshwork was seen nowhere except in the lower angle, where only its anterior portion was visible. In the left eye the angle was everywhere open, though narrow, and a filtration area was visible in the cleft.

The following day, after miotics had lowered the tension to 20 mm. in the right eye, outflow facility was found much improved, though still abnormal, and gonioscopy showed in the right eye an irregularly narrow cleft separating filtration area from iris.

Peripheral iridectomy was done on the right eye (March 9, 1951). Three months after operation, outflow facility in the right eye was in the glaucoma range and was normal in the left eye, with respective tensions of 25 and 24 mm. without treatment. Gonioscopy showed the right iris to be flat; three-fourths of the angle was found free of the small, tent-like peripheral anterior synechias, which were seen irregularly disposed in the remaining one-fourth of the angle.

During the first eight months following surgery, tension in both eyes remained in the range of 17 to 22 mm., without miotics. Since that time the patient has been followed by the referring physician; he has been asymptomatic, and tensions have been normal.

Case 3.—A man aged 66 was first examined by one of us (P. A. C.) on Dec. 16, 1953. As early as November, 1940, he had consulted another oculist for pain in his eyes; at that time vision with correction had been 6/6 in each eye. There was possible glaucomatous cupping of the left nerve head, and a lower Bjerrum scotoma was found in the central field, as well as nasal contraction of the peripheral field, left eye. Tensions were 35 and 48 mm. Hg (Schiøtz) in right and left eyes respectively.

In December, 1940, an Elliot trephine was done on the left eye because tensions had remained in the upper 20's or low 30's with miotics. (Ever since, the left eye has maintained a succulent bleb; its tension has never been above 20 mm.; the field defect has remained stationary, and no miotics have been required. Vision remains 6/7.5 in spite of mild cortical lens changes.)

Between 1940 and 1953, the right eye showed occasional tension rises to as high as 31, 50, or 35 mm. Accordingly, pilocarpine was stepped up in strength and frequency of administration. In October, 1953, use of drops was stopped for 36 hours for evaluation of the glaucoma in this eye. Vision was measured at 6/6; tension, at 53 mm. Outflow facility was demonstrated by tonography to be markedly impaired. The cornea was clear, the anterior chamber shallow, and the nerve head pale but not pathologically cupped. The visual field was normal. Gonioscopy showed a moderately convex iris with a 4 mm. mobile pupil. The angle appeared closed through 80% of its circumference.

Because the tension could be normalized and the angle opened (as seen gonioscopically) by miotics, peripheral iridectomy with sweeping of the angle was done on the right eye on Dec. 18, 1953. Ever since, the tension in this eye has remained in the upper 'teens or low 20's, without the use of miotics.

Evaluation on May 24, five months after operation, revealed vision in the right eye to be 6/6; tension 23 mm. Facility of aqueous outflow was just within the normal range. Gonioscopy showed a relatively flat iris with anterior chamber deeper than before operation. The angle was everywhere open except for peripheral anterior synechias coming forward to Schwalbe's line at 5 o'clock and again at 8 o'clock, and one area of forward iris attachment covering the posterior meshwork. At least 70% of the angle was considered functionally open and of moderate width.

CONCLUSIONS

In subacute angle-closure glaucoma, aqueous outflow is obstructed by apposition of iris and filtration meshwork; a rise in intraocular pressure results, but the pressure increase is less than that accompanying acute angle-closure glaucoma, in which apposition is generalized and complete, or nearly so. Although in the early stages of subacute angle-closure glaucoma the filtration apparatus is unimpaired and the eye may return to normal between attacks, nevertheless, after repeated attacks in some persons part of the angle remains closed by peripheral anterior synechias. If the circumferential extent of peripheral anterior synechias is considerable, tension can no longer be normalized by miotics, and base pressure rises; or the tension may remain permanently elevated in spite of miotics if the peripheral anterior synechias occupy a large portion of the angle.

In early cases of subacute angle-closure glaucoma, any significant tension rise, occurring under faithful miotic treatment, justifies surgical intervention; operation should not be so long postponed that loss of function is allowed to occur.

In early cases of subacute angle-closure glaucoma a hole through the iris will effect a cure. In cases moderately advanced but with an angle which can be at least partly opened and tension normalized by miotics, peripheral iridectomy, plus continued use of miotics, will usually control the tension. In far-advanced cases, a filtration operation may be necessary.

Because it is simpler and safer than a filtration operation, peripheral iridectomy is the operation of choice for early and moderately advanced cases of subacute angle-closure glaucoma. Filtration operations, with their far greater hazard, should be reserved for those eyes which have not been helped by, or are too advanced for, peripheral iridectomy.

It is vital that wound closure be tight in order to avoid the hazards of a flat anterior chamber. The ab externo approach is preferable, and the resulting wound should be the

shortest through which a small portion of peripheral iris can be delivered for excision.

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Psychogenic Ocular Symptoms

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Many writers have used the term ocular neuroses to describe neurotic ocular symptoms. This usage is highly inaccurate and, by ignoring the complexities of character structure from which all neurotic symptoms arise, has led to fanciful discussions of whether ophthalmologists may not cause or cure ocular neuroses.[1] Depending on whether or not a physician is psychiatrically well informed and emotionally well balanced, he may aggravate or ameliorate neurotic tendencies, but he does not cause or cure neuroses by his method of handling the ocular symptoms. I shall describe in its proper context an asthenopia of neurotic origin which I "cured," only to find that a urethritis of neurotic origin had taken its place.

A knowledge of psychiatric and psychoanalytic theory is of immense value to any physician. In spite of the maze of conflicting propositions to be found in these theories, such knowledge creates the frame of thought in which to appreciate how much of human feeling and action is psychically determined by the entire life experience, and particularly by the experiences of the early years. It is possible to achieve a general understanding of human beings within the normal range, as well as of the abnormal, and of those tottering on the edge of normality. Equally important is self-knowledge. The doctor-patient relationship is badly strained if the doctor is unaware of, or is unable to analyze and control, his own tendencies to impatience, intolerance, contempt, and hostility.

It is truly amazing how irrational we all are. Strecker and Appel [2] believe that if every one could modify behavior by thought 25% of the time, this world would be vastly improved. "Disorder of intellect happens much more often than superficial observers will easily believe," wrote Samuel Johnson, who was himself a lifelong sufferer from nervous tics and periods of deep depression.

THEORETICAL CONSIDERATIONS

The problem of neurosis must have plagued man since his nervous system reached its present level of sensitivity. It may have plagued him even before, since there have been reports of neurotic signs experimentally induced in laboratory animals. For the more obvious form of hysteria the ancient Greeks had a word. It was attributed to a displacement of the uterus and found most frequently in elderly virgins and young widows.[3] The later Greeks, the Romans, and the peoples of the East suffered from the machinations of demons. The mediaeval Christians suffered from the Devil himself.

The rebirth of critical thinking which was the Renaissance led to a more careful examination of neurotic characteristics and opened the way to our modern concepts. In the 17th century Robert Burton [4] wrote:

> No sooner are their eyes open, but, after terrible and troublesome dreams, their heavy hearts begin to sigh: they are still fretting, chafing, sighing, grieving, complaining, finding fault, repining, grudging, weeping. . . . But giving way to these violent passions of fear, grief, shame, revenge, hatred, malice, &c. they are torn in pieces . . . and crucifie their own souls. . . . A common fault of melancholy persons [is] to say their symptoms are greater than they are . . . and to be more troublesome to their physicians than ordinary patients.

By the 18th century there was a beginning appreciation of the depths of the human mind. Leibnitz [5] wrote of perceptions which enter the mind without conscious awareness. In the 19th century, Lecky [6] wrote:

> Not only are facts retained in the memory of which we are unconscious, the mind itself is also per-

petually acting—pursuing trains of thought automatically, of which we have no consciousness.

Oliver Wendell Holmes[7] read both Leibnitz and Lecky and developed their ideas in his own papers.

The flow of thought is, like breathing, essentially mechanical and necessary; but incidentally capable of being modified to greater or less extent by conscious effort. Our natural instincts and tastes have a basis which can no more be reached by the will than the sense of light and darkness, or that of heat and cold. . . . There are thoughts that never emerge into consciousness, which yet make their influence felt among the perceptible mental currents, just as the unseen planets sway the movements of those which are watched and mapped by the astronomer.

The greatest single contribution to the understanding of the human mind came from Sigmund Freud, at the end of the 19th century, with his introduction of psychoanalysis. Whatever modifications time may bring to his theories, the fundamental principles seem destined to remain. These principles comprise the doctrines that our mental processes are determined by unconscious motivation as much as, or even more than, by conscious motivation, and that the nature of the motives which drive us is largely emotional.

Freud thinks of the mind as divided among the ego, the id, and the superego. The ego is that part of our conscious awareness that entertains only the personally and socially acceptable desires. The id contains all those untutored, uncivilized instinctual desires which cry for expression without regard for the dictates of experience, of common prudence, or of moral standards. The superego represents the ideal of thought and conduct instilled by parents and society during the formative years. It is the conscience which Plato, the Stoic philosophers, and the Christian theologians considered innate. It is the acquired sense of right and wrong which Aristotle, and the Epicurean and utilitarian philosophers, believed to have evolved slowly in human society and to have been taught by one generation to the next.[8]

The energetic emotional drive from the id is the libido, and Freud considers the libido as expressing sexuality in such a large sense that it includes the wish for all forms of sensual and emotional pleasure. When the id impels the ego to conduct unacceptable to the superego, the superego makes its objection felt by creating a formless, unreasoning fear called neurotic anxiety, or a sense of guilt. If the superego approves the id impulse but external circumstances prevent fulfillment, the id may react with a strong resentment against individuals and society, which is itself punished by the superego with neurotic anxiety. When id and superego are in accord and external circumstances favorable, happiness and contentment result for the moment. For no one, of course, can the ideal situation remain constant.

This mechanism torments us all, for it is based on the drive of human instincts. Those who have good emotional balance repress the improper suggestions from the id, endure the frustration, and thus relieve themselves of the neurotic anxiety. Unfortunately, the repression of the id may itself produce some anxiety. Others who, by reason of an unfavorable heredity or childhood situation, have libidinal drives too powerful to overcome are not able to make this adjustment. They may escape from reality and anxiety into a world of fantasy which is psychosis, or they may express the libidinal desires in disguised or rationalized forms intended to deceive the ego and superego as to their true nature. These forms are the neurotic symptoms.

One blighting childhood situation which Freud presents as practically universal is well known as the Oedipus complex. Boy loves mother and fears and resents father as a rival. Girl loves father and fears and resents mother. These feelings are carried unconsciously into adulthood with varying degrees of intensity, to modify the relations between the sexes. There would seem to be no escape and no complete cure.

In later writings, Freud introduced a new instinctual drive from the id to explain the vast amount of hostility and aggression in this world. In contradistinction to the libido, or life instinct, he postulated a destructive, or

death, instinct. This, like the libido, is constantly seeking expression and if it cannot find a direct or disguised or socially acceptable expression against others, must be turned inward upon the self.

From all this the theorists of the Freudian school have assigned three motives to neurotic behavior which are present in every neurosis, though the forms of expression may be legion and their true significance hidden from the subject.

There is the motivation of aggression. The neurotic succeeds in hurting those who must live and deal with him in a variety of ways by complaints, by demanding attention and sympathy and care, by causing worry, and by incurring expense. This expresses a hostility which never found a direct outlet. The original incident or situation arousing hostility has occurred in childhood, when the defenseless youngster was too weak to retaliate or too afraid of losing affection and protection. Thus, the hostility is often directed against father, mother, brother, or sister, or against some one now identified as one of these. A wife may take the place of a mother. Some one in authority may take the place of the father.

The second motivation is one of self-punishment. Conscious of guilt, the neurotic seeks escape from the condemnation of the superego by expiation. The death instinct is turned inward and if allowed complete expression would proceed to suicide, the ultimate in self-punishment. However, if the life instinct is sufficiently strong or there is enough outward release of hostility, the destruction is confined to impairment of function by way of neurotic symptoms, psychosomatic ills, or purposive accidents. When one is angry and unable to express anger, it is unwise to drive a car or shave with a straight razor.

There is another adaptation of the death instinct which is particularly pertinent to our subject. The generalized sense of guilt may be focused on part of the body particularly associated with the forbidden instinctual drive. Kinsey [*] has tabulated the modes of sexual arousal obtained through visual stimuli and found them of considerable importance, especially in men. Neurotic eye symptoms may reflect this and the visual function carry the burden of guilt.

The third motivation is that of self-love and self-glorification. Libido normally destined for external persons, objects, or social institutions is turned toward the self, and the neurotic, preoccupied with the self, gives his affection only to the self. He takes pride in his afflictions, dramatizes himself as a martyr, and enjoys being the center of attention for relatives, neighbors, nurses, and doctors.*

The basic philosophy of Freud's system is rather discouraging. Horney [13] points out that instincts cannot be eradicated. At best, the life instinct can be managed only by partial frustration, and the death instinct, only by turning outward, to the detriment of others, or inward, to the damage of the self. Life itself becomes a struggle between life and death instincts which involves the individual, and all mankind as well. Freud [14] admits that for humanity he has no consolation to offer, though he hopes for the best.

Menninger [15] is more optimistic. He believes that in the mature individual self-destructive tendencies disappear and externally directed aggressiveness is aroused only by actual dangers. Such emotional balance is the very essence of maturity and the goal of the process known as "growing up." Adult neurotics face their difficulties in the helpless or inadequate manner of the child.

The final expression of self-destruction is suicide. If, however, a psychological compromise is possible, one part of the body, such as the eye, may be substituted for the whole. The severest attack on the eye is complete destruction of the organ by self-mutilation. This occurs among psychotic patients. A less severe attack results in suppression of vision, as in hysterical blindness. The least severe, and by far the commonest attack, is the impairment of vision by means of a host of neurotic symptoms which baffle the attending physician.

* References 10, 11, and 12.

While the selection of the eyes for attack is often determined by the association of vision with the neurotic anxiety, I have found in my cases that the selection may appear to have only a superficial basis. To a neurotic character ocular disease or trauma may direct attention to the eyes. Articles in popular magazines may suggest reasons why the eyes should be the logical focus for suffering. Also, it may seem to the patient that visual disability is the best available means of withdrawing from an intolerable situation. A deeper connection may be present, but its detection would require extensive psychiatric study.

DESTRUCTION OF VISION

The story of Oedipus contains more than the situation which gave his name to the famous complex. It depicts the simple logic by which the mind finds it fitting and proper that visual sin, or violation of taboo, should be punished by loss of vision, and thus it illustrates the psychological mechanism of many ocular neurotic symptoms.

When the King of Thebes learned of a prophecy that his son would grow up to kill his father and marry his mother, he abandoned the infant Oedipus in the mountains. Found and raised by the King of Corinth, Oedipus was informed of the prophecy by the oracle at Delphi when he came of age. Believing his parents to be the King and Queen of Corinth, he left home in order to escape his fate and journeyed to Thebes. On the way he met and killed his father, the King of Thebes, in a roadside quarrel. On reaching Thebes, he married his mother, the Queen Jocasta, became king, and by his mother had four children.

In time this unfortunate pair discovered their true relationship. Jocasta's sense of guilt was the greater, for she committed suicide by hanging. Oedipus made a psychological compromise and destroyed only the visual symbol of guilt by stabbing his eyes with a brooch from Jocasta's dress, crying out, "You have looked enough upon those you ought never to have looked upon."[16]

This cry of Oedipus may be taken to refer to the sight of the children he had sired by his own mother, but, in addition, there is reason to believe that the sight of a naked parent of either sex was considered taboo among some of the ancient Mediterranean peoples.

After Noah had weathered the flood in his Ark, he settled down with his three sons to raise a vineyard.

> And Noah began to be an husbandman, and he planted a vineyard: And he drank of the wine, and was drunken; and he was uncovered within his tent. And Ham, the father of Canaan, saw the nakedness of his father, and told his two brethren without. And Shem and Japheth took a garment, and laid it upon both their shoulders, and went backward, and covered the nakedness of their father; and their faces were backward, and they saw not their father's nakedness.[17]

When Noah recovered consciousness, he degraded the erring son, who had broken the taboo, to the status of a slave.

Oedipus and Noah are creatures of folklore; but folklore, myths, and fairy tales reflect the ancient ways of human thinking. To the peoples who created and preserved the story of Oedipus his action was a natural one under the circumstances. The same mode of thought is found in the story of Lady Godiva and the blinding of Peeping Tom.

Lady Godiva, a legendary 11th century wife of the Lord of Coventry, rode naked on horseback through the town in order to fulfill literally her husband's facetious requirement for the lowering of taxes. A grateful people kept indoors with blinds drawn and refrained from looking, but

> One low churl, compact of thankless earth,
> The fatal byword of all years to come,
> Boring a little auger-hole in fear,
> Peep'd—but his eyes, before they had their will,
> Were shrivell'd into darkness in his head,
> And dropt before him.[18]

The possibility that the lady was conscious of an attractive figure, and therefore had some regrets that no one did see her, would have no bearing on the case. Sin, like beauty, is in the eye of the beholder.

Through the years the penalty for peeping has not changed in the popular mind. An Arabian 16th century manuscript warns that looking into the cavity of the vagina is injurious to the eyes, and relates that, in the opinion of his contemporaries, Hacen ben Isehac, Sultan of Damascus, lost his sight for this reason.[19] According to Pennsylvania German belief, a man will be struck blind if he looks up into a tree while a woman is in the tree.[20]

This same folk attitude is expressed in the Gospel according to St. Matthew [21]:

Ye have heard that it was said by them of old time, Thou shalt not commit adultery: But I say unto you, That whosoever looketh on a woman to lust after her hath commited adultery with her already in his heart. And if thy right eye offend thee, pluck it out, and cast it from thee; for it is profitable for thee that one of the members should perish, and not that thy whole body should be cast into hell. And if thy right hand offend thee, cut it off, and cast it from thee: for it is profitable for thee that one of thy members should perish, and not that thy whole body should be cast into hell.

There have been psychotics who found this passage so applicable to themselves that they acted upon it. When Marco Polo, in the 13th century, reached Baghdad on his way to the court of Kublai Khan, he was told of just such a person. A pious cobbler had yielded to sinful thoughts when the leg of a young woman was exposed as he fitted her with slippers. Recollecting the 18th chapter of St. Matthew, he scooped out his right eye with "an instrument of his trade," presumably a shoemaker's awl.[22]

This tale comes on dubious authority, but there are modern parallels. A case was reported from France in 1888 of a 39-year-old woman who read the exhortation, "If thy eye offend thee, pluck it out," and enucleated one eye with a meat hook.[23]

In 1938 a similar case was reported by the press in this country.

Merced, Cal., Aug. 24 (AP).—A story of how his wife, obsessed with the idea she had sinned, chopped off her left hand and gouged out her right eye was told from a jail cell here tonight by Woodrow Harwell, 20-year-old Texas cotton picker.

District Attorney F. A. Silveira quoted Harwell as saying he and his two young stepsons knelt in prayer yesterday afternoon in their one room cabin while his 26 year old wife read from the bible.

She read Matthew 18:8, 9.

Mrs. Harwell rose from prayer, her husband related, saying her left hand offended her and she wished forgiveness for her sins. She went outside the cabin, Harwell said, and gouged out her eye with a pair of scissors. Then she placed her hand against a cement pipe and hacked it off with an axe. Harwell said she struck her wrist three times before she severed the offending hand.

Such incidents bring to mind a remark of Oscar Wilde. He said that when he considered how much damage the Bible had done, he despaired of writing anything to equal it.

SUPPRESSION OF VISION

Hysterical blindness may be complete or partial, binocular or monocular. Central vision may remain good while the visual field shows the most bizarre changes, which vary from one examination or examiner to another, or there may be any degree of amblyopia associated with the field changes. Nevertheless, the pupils react to light, and light stimuli cause normal alterations in the electroencephalographic pattern. Loss of vision commonly persists from a few hours to a few months, though a child of 10 years was reported to have been hysterically blind for four years.[24]

As late as 1854, disturbance of the uterus was given in a textbook of ophthalmology as one of the causes of hysterical blindness.[25] The ancient conceptions die hard.

Because such blindness may be induced in suggestible subjects under hypnosis, it has been considered possible that in neurosis the unconscious mind suggests blindness to the conscious mind as the hypnotist does to his subject.[26] Furthermore, it is obvious that these patients do, in a sense, see. They show an amazing lack of concern for their predicament, and a surprising ability to circumnavigate impeding objects. They may write words which they do not consciously see, but which could not be written if the subconscious mind did not follow the action.[27] If an object is held before an hysterically blind eye, the pa-

tient, after being hypnotized, will be able to describe the object.[24] Moore [28] saw a girl abruptly cured of blindness when a live frog was suddenly thrust in her face. Thus we might say that the conscious mind suffers a suppression of vision, the subconscious mind does not, and a psychic jolt may break down the dissociation.

Freud [29] has suggested several related psychic mechanisms which may explain many, though not all, instances of hysterical blindness. When a forbidden sexual interest becomes deeply involved with the faculty of vision, the force of the required repression may suppress both the sexual interest and the vision. In addition, the repressed impulse is taking its revenge upon the ego, and the superego is exacting self-punishment.

The conversion hysteria of soldiers on active duty, by which they escape overwhelming sights and situations, seems quite unrelated to these subtle explanations. So do many cases in civilian life.

A 17-year-old girl, four months pregnant, was admitted to the Pennsylvania Hospital after sudden loss of vision. Since she was unmarried, her family had been subjecting her to constant reproach and forcing her to do all the manual labor of the household. On admission vision was 6/60 in each eye. Reassurance and a calm acceptance of her breach of the conventions brought vision to normal after a few weeks' stay in the hospital.

Alexander and Healy,[30] in the course of psychoanalyzing a young woman shoplifter, learned that in childhood she escaped sordid physical surroundings, a hostile mother, and an unhealthy emotional relationship with her father by "phantasing" and playing that she was blind. If such an escape can be sought consciously, it is not surprising that the emotionally unstable seek it subconsciously.

The involvement of the eye in hysteria may also be entirely fortuitous. A 31-year-old woman was knocked down by a blow of her husband's fist, and a laceration was inflicted by a large ring 2 in. above the right eyebrow, requiring one suture. Edema and ecchymosis of the upper right eyelid closed the right eye. When the eye finally opened, after a few days, she found the vision of the right eye extremely blurred. Under the observation of an ophthalmologist vision gradually improved during six weeks, but fresh outbursts of temper on the part of the husband against his wife's assumption of invalidism caused a relapse.

At this point the patient consulted me. The vision of the right eye was 6/15, and that of the left eye 6/6. The right peripheral field was constricted 30 degrees regardless of size of test object or distance from object to patient. The left field was full. I reassured the patient and explained to the husband that a "nervous disease" was actually present. The terrible temper was controlled, and four months from this time vision was 6/6 + and the visual field was full in both eyes.

This amblyopia served the truly useful purpose of restraining the husband's violence. It was also an expression of resentment for numerous insults and of guilt for having married a second time while cherishing an attachment for the deceased first husband.

Hysterical blindness appears in a footnote to history. The official German account ascribes Hitler's blinding in World War I to poison gas. Foster Kennedy [30] writes that a friend, in whom he has absolute confidence, inspected the German army medical record in 1931 and found the diagnosis to be hysterical amblyopia. In 1934, after Hitler came to power, the record had disappeared.

IMPAIRMENT OF VISION

Vision is impaired, as distinct from being suppressed, by the lesser hysterical manifestations, such as hysterical ptosis, blepharospasm, blepharoclonus, convergence excess or insufficiency, convergent strabismus, cycloplegia, night blindness, and external pseudo-ophthalmoplegia. Weiss and English [31] also consider miners' nystagmus as psychogenic.

Anomalies of iris movement, such as miosis, mydriasis, anisocoria, or hippus, may accompany any of these evidences of hysteria, as well as anesthesia of the conjunctiva or cornea.

In a class by themselves are those malingerers, chiefly young women, who introduce damaging material into the eyes for psychopathological purposes. Many substances have been so used. Duke-Elder [32] mentions lye, lime, sand, ashes, aniline pencil, pepper, soap, tobacco, ipecac, and juice of the castor oil bean. On occasion, impairment of vision has ended in destruction of vision.

Much commoner are the neurasthenic symptoms of itching, burning, lacrimation, photophobia, eye fatigue, headache, light flashes, cyclospasm, blurring, rings around electric lights, monocular diplopia or polyopia, spots before the eyes, and a vast assortment of aches and pains in and about the eyes, often radiating to other parts of the head and to the neck.

Undoubtedly, many patients derive a sense of protection from wearing glasses which interpose their fragile strength between tender sensibilities and a harsh external world. Weak spheres, or even plane glass, may serve this purpose. Tinted glasses, graded in color to suit the temperament, are also popular for this reason. I have examined several inmates of a psychiatric institute who wear dark glasses indoors and out as a measure of emotional protection and withdrawal.

Young children who wish emotional support by identifying themselves with favorite playmates or relations who wear glasses often develop eye complaints and weep when told that they do not need glasses. The onset of squint may come with an emotional crisis in an unhappy child, and the cure by orthoptics may mainly reflect the sympathetic attitude of the orthoptist.[33]

Every practicing ophthalmologist is continually meeting these patients. According to Strecker and associates,[34] it has been estimated that 40% to 50% of those who consult general practitioners have neurosis as their major difficulty. Bahn [35] reviewed a series of 400 consecutive office patients in ophthalmic practice, 215 men and 185 women. In his opinion, a neurotic factor capable of effecting symptomatic recovery existed in 301 cases (75%). However, since in more than half of Bahn's patients the neurosis was a minor factor, his percentage is not strictly comparable to that of Strecker for general practice. Adler [36] states that neurotic symptoms are probably commoner in the eye than in any other organ. In contrast to civilian life, Birge [37] found ocular symptoms of low occurrence in war neuroses, which are less dependent on a markedly neurotic character or on sexual conflict, but are more the outgrowth of the immediate situational stress.

In the 1917 edition of Mary Baker Eddy's "Science and Health" there are 83 testimonials to the curative powers of Christian Science. Of these believers, 17 (20.5%) had been able to dispense with their glasses or believed themselves cured of serious eye disease. Another evidence of the high frequency of ocular symptoms among neurotics is the large sale of books advocating the Bates system of exercises for the cure of refractive errors, muscle imbalance, strabismus, cataract, and glaucoma. The publisher's advertisement claimed that more than a half-million copies of Peppard's "Sight Without Glasses" had been sold. Aldous Huxley's "The Art of Seeing" reached its 18th edition.

These methods of faith healing act by allaying neurotic anxiety. Christian Science denies the material existence of disease and imposes the task of reading Mrs. Eddy's book. Since large portions of the book consist of verbiage without discernible meaning, the ordeal is not unlike that endured by the disciple of Bates, who reads short stories with the book held upside down, blinking continuously as he proceeds from the lower right-hand corner of the inverted page. In these ways, the neurotic convinces himself that he has earned the right to use his eyes, and that under such authoritative guidance use will not harm them. Guilt is expiated by such activities as long as they are continued. I suspect that the strenuous "health routine" of diet and calisthenics prescribed by Bahn [35] acted much in same way, for of the eight successfully treated patients reported in detail, six relapsed when they stopped following the routine. The other two appear to have continued with it.

To the exercises of Bates, Huxley added an element of Indian mystical philosophy, with its emphasis on the annihilation of desire and the merging of the conscious self into an all-pervading "over soul." Mysticism is the deliberate attempt to achieve a sense of unreality, and this refined form of self-destruction makes a great appeal to the intellectual neurotic.

One can only speculate on the reasons why the eye is so prominent in neurosis. Certainly, the association between sin and vision is widespread and, apparently, does not cease with blindness. Among the Ch'uan Miao, a Mongolian people of Central Asia, there is a prescribed incantation for driving out the demon that punishes sin by causing pains in the eyes.[38] In 1936 the Braille Club for the blind of San Diego protested against the establishment of a nudist colony in the community.[39]

Kinsey [9] has indicated not only that much sexual satisfaction is obtained through vision but also that the amount varies among individuals. In the neurotic perversion of voyeurism sexual satisfaction is derived entirely through vision. Perhaps those who would normally obtain much of their sexual satisfaction visually are, when subject to neurosis, more prone to ocular symptoms.

One of my patients, a man of 32, suffered from burning of the eyes and blurring of vision for several days after sexual relations with his wife, which occurred about once a month. In another instance, a man of 30 complained of periodic ocular burning and aching. The eyes appeared normal; vision was 6/6 in each eye; the muscle balance was well within normal limits, and the refractive error found under cycloplegia was so slight that I did not prescribe glasses.

I then reviewed the history more carefully and asked the patient whether his symptoms were connected with any nervous tension. He admitted that he occasionally left his wife and two children, of whom he was very fond, to spend the night with another woman. On the days immediately following his dereliction ocular symptoms were most pronounced. He felt that he must have, or at least should have, a gonorrheal infection, for he had read that this venereal disease was particularly dangerous in the eye.

I explained to him that he must either so alter his conscience that he would not be upset by extramarital activity, which I admitted would be difficult, or that he must abstain from relations with his paramour, which he admitted would be very difficult. Actually, he needed a psychiatrist to unearth the neurotic trend which made so impractical a matter as the possession of two women on a limited income and in our culture appear desirable.

The man seemed impressed with this advice and one month later pleased me greatly by reporting that he had been at home every night since his last visit to my office and that his eyes were entirely comfortable. Several months afterward a urologist requested the patient's ocular history. The romantic fellow was now convinced that he had a gonorrheal urethritis, though there was no evidence of the disease. I presume he had taken to going out at night again.

Menninger [12] gives a classically Freudian instance of neurosis with ocular symptoms. A young woman of 24 had been treated unsuccessfully for 12 years because of ocular pain and aching. Investigation revealed that the onset occurred after the death of a brother whom she had hated and envied. At one time she had gone to his room to look at him while he slept in order to see the anatomical difference between herself and him. The death of the brother crystallized her sense of guilt for her feeling of hatred, and guilt for the peeping incident directed the self-punishment to her eyes.

PSYCHOSOMATIC OCULAR DISEASE

It is appropriate to the importance of the subconscious mind that it should have a nervous system peculiarly its own.

Ranson [40] has defined the autonomic nervous system as "that functional division of the nervous system which supplies the glands, heart, and smooth musculature with their efferent innervation." The conscious mind has no control over this system. Its activity is

stimulated by pain, extremes of temperature, lack of oxygen, infection, emotional stress, and psychic trauma. Harrington [41] quotes Cannon to the effect that if no action follows the bodily changes created by excitement, worry, and anxiety through the action of the autonomic nervous system, the organism may be profoundly upset. Thus, a mechanism is established by which we may explain somatic changes secondary to the repressions and frustrations of a neurotic state of mind.

In 1939 Gifford and Marquardt [42] reported eight cases of macular edema in young or middle-aged adults with no generalized hypertension and reviewed similar cases previously reported. Because of the absence of inflammatory signs and the presence of demonstrable vasomotor instability, they suggested that the cause was the constriction of a number of small vessels supplying the macular region, and they called the condition central angiospastic retinopathy. Some of these cases recovered completely, but others retained permanent macular defects with diminished vision.

In 1946 Harrington [43] was able to report 40 cases of central angiospastic retinopathy which occurred among Navy personnel during World War II, involving one or both eyes and leading to a permanent defect in some. All had a history of emotional strain, and all showed positive reactions to tests for vasomotor instability. Harrington believes that a similar spastic etiology is behind the amaurosis fugax which he found among the homesick, worried, or combat-fatigued members of the armed services, among medical students at examination time, and among patients with neurocirculatory asthenia.

Emotional disturbance also plays a part in causing the vasoconstriction of Raynaud's disease,[43] a disease which may involve retinal arterioles and even the central artery.[44] Harrington concluded that psychic trauma in susceptible persons can produce organic changes in the eye. Weiss and English [31] endorse this view and agree with Zeligs that such patients should have not only antispasmodic therapy but psychotherapy as well.

Harrington also found that the incidence of ophthalmic migraine with scintillating scotoma and transient homonymous hemianopsia very high in the armed services and considered this another instance of vasomotor instability. The precipitating factor was nearly always psychic trauma. Weiss and English [31] were impressed by finding that migraine patients tended to have a particular type of neurotic character. These patients were subject to compulsions and were unable adequately to express hostile feelings, and there was impotence among the men and frigidity among the women.

Menninger [12] describes a man reported by Groddeck in whom recurrent retinal hemorrhages appeared to have a psychogenic basis. These hemorrhages had continued for years and were more apt to occur in the autumn, and at the sight of a cross or crucifix. It was finally elicited that in the autumn, at the age of 8, he had accidentally knocked over a wayside crucifix and broken the figure of Christ. He also remembered that in the pious village where he spent his childhood there had been a blind man who was believed to have been blinded by God because he never went to church. Since leaving his childhood home, the patient had severed all religious connections and scoffed at religious belief. Menninger considers this an instance of guilt and self-punishment, with the memory of the blasphemous blind man directing the symptoms to the eyes.

"Bloody tears" occur in several rare conditions, but they are particularly weird in hysteria. In a case reported by Hyuck [32] in 1932, a woman wept tears of blood for her dying Saviour each year on Good Friday.

Klauder [45] spent two weeks observing a case of stigmatization in which bloody weeping occurred. This young woman had developed slightly elevated, discolored lesions on both sides of her hands and feet, over the heart, and at three places on the scalp eight years previously. A religious ecstasy set in between 11 and 12 p. m. every Thursday and lasted until Friday afternoon. During this time blood-tinged tears ran down her face,

to clot on the chin and neck. On Friday one or more stigmas would ooze blood. Only on Good Friday would all the stigmas bleed. Microscopic examination of the fluid in the lower conjunctival fornix demonstrated the actual presence of blood. The probable source of such bleeding is the palpebral conjunctiva.[32]

The stigmas correspond to the five wounds of Christ, though when the wound is on the left side of the chest instead of the right, it must reflect the impression gained from a painting of the crucifixion in which the wound on the right side of the body appears on the left side of the picture. The scalp lesions correspond to the crown of thorns. The symbolism of the bloody tears is not so clear. They might represent a confusion of two biblical verses, "Jesus wept,"[46] well known as the shortest verse in the Bible, with, "And being in agony he prayed more earnestly: and his sweat was as it were great drops of blood falling down to the ground."[47]

It is well known that an emotional crisis may be a precipitating factor in attacks of acute simple glaucoma. Inman[48] reported several cases in which the occurrence of such attacks on an anniversary having painful emotional significance pointed to chronic anxiety as a precipitating factor. Psychoanalytic and tonometric study of a woman with chronic simple glaucoma showed a definite correlation between pressure and emotional tension.[31] To explain this relationship, we need only refer to the probability of control of intraocular pressure through the parasympathetic division of the autonomic nervous system.[49]

Sugar[50] expresses the generally accepted opinion that the neurotic factor is not the cause of glaucoma. It can precipitate acute attacks only when chronic simple glaucoma is already present, or there is a glaucomatous predisposition.

CONCLUSION

The primary function of the ophthalmologist is to determine the presence of organic lesions or visual malfunction and to give whatever treatment is possible. The physical examination should be complete and careful no matter how neurotic the patient may appear to be, for personality changes occur in dementia paralytica, multiple sclerosis, arteriosclerosis, and intracranial space-taking lesions.

Furthermore, any physical disease may have a large neurotic component. Neurotics use organic disease as a shield of defense, as a weapon of offense, and as a glorification of the ego. It is necessary to form some estimate of the relative importance of mind and matter in each case and to remember that the two are inextricably connected and should not be approached separately.

No doubt it means a sacrifice of time and a trial of patience properly to handle these people. They talk interminably. They bring to the office written lists of symptoms to recite and of questions to ask. They phone later to add a forgotten detail. They write long letters containing progress reports.

These are symptoms of the disease, and a physician cannot logically reject a patient because he finds the symptoms objectionable. Such patients are in distress. It is not true that they enjoy suffering. Neurotic symptoms are endured in an effort to escape neurotic anxiety. For the neurotic it is the choice of the lesser of two evils.

The basic cause of anxiety cannot be uncovered without expert psychiatric study, but any physician can achieve a reduction of nervous tension. Bearing in mind the exaggerated sensitivity and suggestibility characteristic of neurotics,[51] he should take the patient seriously and make his examination so obviously thorough that his assurances that no serious organic disease is present carry as much conviction as the patient is able to accept. Added worry from misinformation can be removed to a great extent. The patient should know that eyes are not "ruined" by lack of glasses, incorrect glasses, excessive reading, poor illumination, cheap sunglasses, or devotion to television.

When no treatment is indicated for organic disease, I believe that a soothing eyewash is permissible as long as it is clearly

understood that the prescription is only to make the eyes feel better and will not touch the basic problem. A prescription for glasses must be presented to the patient with the same understanding. Patients resent being told they are mental cases, but they do not object to hearing that they suffer from nervous tension. It has an air of respectability.

Strecker [33] has written that the majority of psychoneurotic and psychosomatic patients must be treated by general practitioners and the specialists. To meet this responsibility and to be what Strecker considers the complete doctor, some knowledge of psychiatry is necessary.

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Posterior and Anterior Chamber Aqueous Humor Formation

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Aqueous humor was once thought to be a dialysate of plasma, or to be secreted as such by the ciliary body in a manner analogous to secretion of saliva by the salivary gland. Many observations on aqueous humor, both experimental and clinical, could not be accounted for on the basis of either of these suggested mechanisms of aqueous humor formation. Accordingly, a theory was evolved which envisaged these two processes, secretion and diffusion (dialysis), as taking place simultaneously.*

Recent studies of the chemistry of the posterior chamber aqueous humor [3] have provided additional evidence that aqueous humor is formed by at least two processes and, in addition, have shown that there are two kinds of aqueous humor in the eye: one in the posterior chamber, and another, having a different composition, in the anterior chamber. Much more experimentation is required, however, to elucidate fully the general nature of aqueous humor formation.

Before discussing the present investigation, we shall review some of the factors which should be considered in any complete explanation of aqueous humor dynamics, indicating those factors which are known and based on reasonably sound experimental evidence, and those which require further study.

Abundant evidence is available to suggest that a not insignificant proportion of all constituents normally present in the aqueous humor of the posterior chamber enters from the blood across the several barriers presented by the ciliary processes, and that the resultant fluid flows between the lens and the posterior surface of the iris (lens-iris space) into the anterior chamber. Some of the constituents of the posterior chamber aqueous humor must also be exchanged with those of the vitreous humor and lens.

With regard to the anterior chamber, many experimenters have contributed evidence indicating that various foreign test substances enter the anterior chamber aqueous humor partly from the blood across the iris vessels. Others have shown that exchange of substances takes place between the anterior chamber aqueous and tissues bordering on the anterior chamber. That direct diffusion from the blood plays a part for the normal constituents also is shown by the different composition under steady-state conditions of the anterior and the posterior chamber aqueous humor, especially with respect to anions and nonelectrolytes.[3]

The rate of flow of aqueous humor out of the anterior chamber has been determined for various laboratory animals † and in human beings,‡ and numerical values for the coefficients of transfer of water and various solutes into the anterior chamber have been estimated from the rate of accumulation of these substances. The accuracy of the co-

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* References 1 and 2.

† References 4 through 11.

‡ References 12 and 13.

efficients of transfer, however, has been limited because of the difficulty in estimating rate coefficients from experimental curves which represent several separate processes, and hence involve double or triple exponential functions. This difficulty has been brought out by Palm,[7] who has fitted equations involving double exponentials to experimental data on the turnover of phosphate in the anterior chamber aqueous, thus making it possible to estimate the exchange of the test substance between the anterior chamber aqueous and its environment. Davson § has recently taken into consideration the process within the "aqueous-forming" ciliary cells, and has formulated a double exponential equation to represent the proposed processes involved. Quantitative appraisal of the transfer coefficients is further complicated by the difficulty in assessing the time required for complete mixing of aqueous humor and that required for the substance to pass from the posterior to the anterior chamber.‖

Earlier studies of the renewal rate of the aqueous humor constituents show the weakness of treating the aqueous humor as a whole. It is necessary to consider the processes involved in the formation of posterior and anterior chamber aqueous humor separately. While the statics of the posterior chamber aqueous humor has been studied,[8] direct investigation of its dynamics has not been performed heretofore. However, Palm[10] has studied the renewal rate of phosphates and sodium in the posterior chamber indirectly, by estimating the concentration of these ions present from that present in the iris and ciliary processes, on the one hand, and aqueous humor, on the other.

Clearly, the mode of formation of aqueous humor of the anterior chamber cannot be understood satisfactorily until information is obtained on the fraction of any given constituent which enters by flow from the posterior chamber and that which enters by diffusion directly from the blood through the iris vessels, and possibly other sources ¶ adjacent to the anterior chamber. To date, this knowledge has not been available. The first objective of the present study is to make such determinations, using as test substances a positively charged ion (sodium) and a negatively charged ion (thiocyanate). A correlated objective of this investigation is to determine the rate of flow of aqueous humor based on a concept of aqueous humor dynamics, involving both the posterior and the anterior chamber aqueous.

Little is known concerning the mechanism by which substances enter the posterior chamber. Bicarbonate ions are believed to be produced in the ciliary body from hydroxyl ions and carbon dioxide.[16] It is this ion which has been proposed as being primarily responsible for maintaining the hypertonicity of the aqueous humor,[2] thereby providing the immediate source of energy available for the through-and-through flow. Theoretically, the formation of the negatively charged bicarbonate ions in the ciliary body, with subsequent transfer to the posterior chamber aqueous, could provide the force necessary for transfer of sodium and the few other cations present in the blood against a concentration gradient, while at the same time impeding the passage of anions. However, no direct experimental evidence has been obtained to support this suggestion, nor is there any to indicate how the anions, other than bicarbonate and ascorbate (which seem to represent special cases), enter the posterior chamber. The second objective of this study, therefore, is to obtain knowledge which may serve as a basis for explaining the mechanism of entrance of differently charged ions into the posterior chamber.

For the purpose of quantitatively evaluating the coefficients employed in describing the dynamics of the anterior and posterior chamber aqueous humors, it is necessary to know the concentration of a substance in the posterior and anterior chamber aqueous hu-

§ References 14 and 15.

‖ References 6 and 7.

¶ No attempt will be made in this paper to distinguish between entrance into the anterior chamber from these sources and from the iris.

mors, the concentration in the plasma, and the relation between the flow rate through the pupil and that out at the angle. No one has made direct measurements of the flow rate from the posterior to the anterior chamber, but in a previous investigation [3] one of us (V. E. K.) showed that the osmotic pressure of the aqueous humor of the posterior chamber does not differ measurably from that of the anterior chamber aqueous humor.# This suggests that there is no net gain to, or net loss of water from, the anterior chamber aqueous across the iris, and thus the flow rate into and the flow rate out of the anterior chamber must be essentially identical.

MATHEMATICAL CONSIDERATIONS

Anterior Chamber.—If a substance is presumed to enter the anterior chamber both by flow from the posterior chamber and by diffusion from the blood, for instance, by way of the anterior surface of the iris, and if it is further presumed that the substance is lost from the anterior chamber by flow, the rate of accumulation of such a substance in the anterior chamber is described by the following equation.

$$\frac{dC_{Aq.ant.}}{dt} = k_{flow}C_{Aq.post.} + k_{diff.ant.}(C_{Pl.} - C_{Aq.ant.}) - k_{flow}C_{Aq.ant.} \quad (1a)$$

and at steady state:

$$\frac{C_{Aq.ant.}}{C_{Pl.}} = \frac{k_{diff.ant.} + \left(\frac{C_{Aq.post.}}{C_{Pl.}}\right)k_{flow}}{k_{diff.ant.} + k_{flow}} \quad (1b)$$

also

$$\frac{k_{diff.ant.}}{k_{flow}} = \frac{C_{Aq.ant.} - C_{Aq.post.}}{C_{Pl.} - C_{Aq.ant.}} \quad (1c)$$

where

k_{flow} = coefficient of transfer by flow into and out of anterior chamber

$k_{diff.ant.}$ = coefficient of transfer by diffusion between blood and anterior chamber

$C_{Aq.post.}$ = concentration in the posterior chamber aqueous

$C_{Pl.}$ = concentration in the plasma

$C_{Aq.ant.}$ = concentration in the anterior chamber aqueous

The values for the k's are in reciprocal minutes.

(The exchange of substances between the anterior aqueous humor and the lens and the cornea is disregarded, as are also various time lags between different parts of the system.*)

It is apparent that Equation 1a is closely related to that used previously by us and others.† If none of the substance in question flows from the posterior chamber, i. e., $k_{flow}C_{Aq.post.} = 0$, the equation reduces to that used in previous papers,‡ where it was assumed (for purposes of testing one or another hypothesis) that entrance occurred solely by diffusion.§ Similarly, if none of the substance enters the anterior chamber by diffusion, i. e., $k_{diff.ant.}(C_{Pl.} - C_{Aq.ant.}) = 0$, it is apparent that the equation is analogous to that used previously to represent entrance solely on the basis of secretion,‖ where $k_{sec.}C_{Pl.}$, the coefficient of transfer by secretion from blood to anterior chamber, as used formerly, is analogous to $k_{flow}C_{Aq.post.}$

Posterior Chamber.—In the foregoing mathematical treatment of the dynamics of the anterior chamber aqueous humor, the effect of diffusional exchange with the environment (except the blood) was disregarded. However, in the mathematical treatment of the dynamics of the posterior chamber aqueous humor, failure to take into account diffusional exchange with the environment would be expected to result in serious error. An exact mathematical treatment of the processes involved would require the use of Fick's unabbreviated equation,[6] involving derivatives of concentration gradients which no doubt arise in the vitreous and lens. This would lead to complicated mathematical procedures, the use of which is not justified by the data available. A practical possibility, however, is to treat the environment as a "lumped system" [17] behaving like an amount of stirred fluid, separated

The experimental error involved was approximately 1%.

* Davson,[15] Friedenwald, J. S.: Personal Communication to the authors.

† References 12 and 15.

‡ References 1 and 5.

§ $\frac{dC_{Aq.ant.}}{dt} = k_{diff.ant.}(C_{Pl.} - C_{Aq.ant.}) - k_{flow}C_{Aq.ant.}$

‖ $\frac{dC_{Aq.ant.}}{dt} = k_{sec.}C_{Pl.} - k_{flow}C_{Aq.ant.}$

from the posterior chamber aqueous humor by a membrane.

Thus, if a substance is assumed to be transported into the posterior chamber at a rate substantially independent of the concentration already present in that chamber,¶ whence in part it flows from the posterior to the anterior chamber, and in part diffuses into the environment, such as the vitreous, lens, and any other region bordering the posterior chamber, the rate of accumulation of such a substance in the posterior chamber is described by Equation 2:

$$\frac{dC_{Aq.post.}}{dt} = k_{sec.post.}C_{Pl.} - K_{flow}C_{Aq.post.} - k_{diff.post.En.}(C_{Aq.post.} - C_{En.}) \quad (2)$$

where

$k_{sec.}$ = coefficient of transfer by secretion from blood to posterior chamber.

$C_{En.}$ represents the concentration in the environment, which environment is considered as a "lumped system." Thus, $k_{diff.post.En.}$ is a "lumped parameter" and represents the coefficient of transfer by diffusion from the posterior chamber to the environment.

K_{flow} is the coefficient of transfer from posterior to anterior chamber by flow. (A capital K is used here to differentiate this coefficient from the analogous one in Equation 1a, in which instance a lower case k is used.) While the coefficient in both instances refers to the same flow, viz., from posterior to anterior chamber, the numerical values for K_{flow} in Equations 2 and 3 will be different from the value for k_{flow} of Equation 1a because the coefficient is a complex one involving volume. Since the volume in the posterior chamber is approximately one-fifth of that of the anterior chamber, K_{flow} should be represented by a numerical value five times that of the k_{flow}.

Equation 3 describes the entrance of a substance into the posterior chamber on the assumption that it enters by diffusion from the blood and leaves in part by flow from the posterior chamber to the anterior chamber and in part by diffusion into the environment.

$$\frac{dC_{Aq.post.}}{dt} = k_{diff.post.}(C_{Pl.} - C_{Aq.post.}) - K_{flow}C_{Aq.post.} - k_{diff.post.En.}(C_{Aq.post.} - C_{En.}) \quad (3)$$

It is assumed for the present purpose that at steady state $C_{Aq.post.} = C_{En.}$; hence at $t = \infty$ for secretion, $k_{sec.post.}C_{Pl.} = K_{flow}C_{Aq.post.}$, and for diffusion $k_{diff.post.}(C_{Pl.} - C_{Aq.post.}) = K_{flow}C_{Aq.post.}$, where $C_{Aq.post.}$ represents the steady-state value of posterior chamber aqueous humor concentration.

METHODS

Biological and Chemical.—The rate of accumulation in the posterior and anterior chamber aqueous humors of two test substances was determined in conscious, young adult albino rabbits weighing approximately 2500 gm. The test substances were administered by intraperitoneal injection. Thiocyanate was given as a 1.2% solution of sodium thiocyanate in the following doses: A single dose of 2 ml/kg. was administered in those experiments involving time intervals of less than three hours; for longer time intervals 0.05 ml/kg. additional thiocyanate was given after the first hour at half-hour intervals.

Radioactive sodium (Na^{24}) was injected in the form of isotonic sodium bicarbonate. The solution used had an activity of 4×10^7 counts per minute per milliliter. One-half milliliter was given to each animal in all the acute experiments, and 0.3 ml., to each animal when the steady-state levels were to be determined.

The relative concentrations are calculated on the basis of the amount of the substance present per kilogram of water. In those instances in which steady-state levels were to be determined, no water was given to the animals for six hours previous to or after the injections.

Samples of aqueous humor were obtained from the posterior chamber and immediately thereafter from the anterior chamber using micropipettes and techniques described previously.[3] The eyes were anesthetized topically with tetracaine hydrochloride and in many instances were tapped repeatedly at intervals of one week or longer, provided no signs of inflammation were visible. Comparison of results obtained in animals whose eyes were tapped for the first time with those tapped after a period of one week showed that in the absence of grossly visible inflammation, or abnormally high protein

¶ The processes responsible for such transport are called secretion. The term is being retained until such time as the nature of the processes is sufficiently understood to make appropriate introduction of a more specific word. It is used only in a broad general sense, however, and is analogous to that proposed by Kinsey and Bárány in 1949 in considering transport into the anterior chamber, where it was emphasized that the term implies only a net transport into the anterior chamber without any other physiological implications.

concentrations, use of the same animals over again was without demonstrable effect. Blood samples were obtained by heart puncture; at least three, but no more than five, samples of 2 to 3 ml. were taken per animal; heparin was used as an anticoagulant. In instances in which the variation in concentration in the plasma, after having attained an essentially constant level, exceeded 15%, the results were discarded.

Concentrations of thiocyanate in plasma and aqueous humor were determined in the following manner: An equal volume of 10% trichloroacetic acid was added to the sample, and the mixture was centrifuged. To 0.050 ml. of supernatant was added 0.10 ml. of 7.5% $Fe(NO_3)_3 \cdot 9H_2O$. The density of color of the resulting solution was determined at a wave length of 470 mμ in a Beckman D U spectrophotometer, using microcuvettes and the mechanical adapter described previously.[18]

Aqueous humor contains the equivalent of approximately 0.6 mg. of thiocyanate per 100 ml., and plasma the equivalent of approximately 1 mg. of thiocyanate per 100 ml. All the concentrations of thiocyanate reported in this paper are corrected to take these blanks into account.#

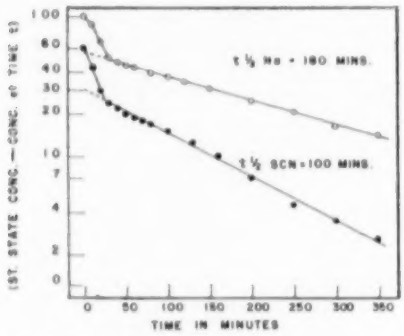

Fig. 1.—Relation of the difference between the logarithm (in per cent) of the steady-state concentrations of sodium and thiocyanate and the concentrations of these substances in the posterior chamber aqueous humor to various times after intraperitoneal injection.

The concentration of radioactive sodium was determined by the usual technique, using a thin window counter and a decade scaler.

Separate experiments, using a standard solution of sodium bicarbonate containing labeled sodium, were performed to show that the counting rate was independent of the volume of solution used in making the count.

Mathematical.—Sliding averages of the data were obtained using six values for each average.[21] The coefficients of transfer were evaluated by numerical integration.

Kinsey and Grant,[19] among others (Davson and Matchett[14]), have previously employed thiocyanate as a test substance in ocular experiments. To determine the amount of thiocyanate bound to plasma proteins, they added known amounts of this substance to plasma and then either ultrafiltered or dialyzed the plasma. The authors found that the concentration of thiocyanate in the ultrafiltrate or in the dialysate was less than in the mother liquid. Similar results were obtained by Davson and associates,[20] who also dialyzed samples of plasma containing thiocyanate. Both groups concluded that approximately 20% of thiocyanate is bound to plasma protein, and therefore corrected all of the data to include only diffusible thiocyanate.

In the present experiments the procedure of ultrafiltration was again performed and a similar result was obtained; however, the observation of an occasional steady-state ratio $\frac{C_{Aq.\,hum.}}{C_{Pl.}}$ (in nephrectomized animals) in excess of 1 led us to search for the cause of the apparent discrepancy. Several fruitless leads were pursued.

We then observed that the distribution of the color-producing material in the aqueous humor and the plasma of control animals, to which no thiocyanate had been given, was different from the apparent distribution under steady-state conditions after injection of thiocyanate. The value for the steady-state ratio $\frac{C_{Aq.\,hum.}}{C_{Pl.}}$ before injection of thiocyanate was approximately 0.5, whereas after injection it was approximately 0.8. This suggested that at least some of the material normally present in rabbit plasma and aqueous humor which produces a color similar to that produced by thiocyanate in analysis was bound to the plasma protein. Thus, any procedure, such as ultrafiltration or dialysis, which concentrates the protein would be expected to raise still further the concentration of the color-producing blank. This was confirmed experimentally by ultrafiltration of normal plasma and plasma taken from nephrectomized animals, many of which showed still greater than normal concentrations of the color-producing material in their plasma. Further experimentation showed that when allowance was made for this color-producing substance, the concentrations of thiocyanate in the mother liquid and ultrafiltrate were so nearly alike that they lay within the experimental errors involved. As a consequence, we concluded that no appreciable amount of thiocyanate is bound to protein; hence no correction was made for nondiffusible thiocyanate in the experiments reported in this paper. The ultrafiltration procedure can be conveniently carried out by placing a sheet of Cellophane over the screen of an ordinary Seitz filter and applying pressure up to 100 lb. per square inch from a tank of compressed nitrogen.

In performing the numerical integrations based on Equations *2* and *3*, the values for the concentration of a substance in the environment of the posterior chamber ($C_{Rm.}$) were estimated in the following manner: The logarithm of the difference between the steady-state concentration (in per cent) and the observed concentration of the test substance in the posterior aqueous at various intervals after injection of the test substance into the animal (Fig. 1) was plotted against time. It is evident that for both thiocyanate and sodium the relation may be approximately represented by two straight lines, suggesting that at least one fast and one slow process are operative in controlling the filling of the posterior chamber. The considerably lower slope observed for both substances at times in excess of 30 to 40 minutes suggests that the slower of these processes (which may be a complex one) becomes dominant after this time. The physiologic equivalent of this slower process no doubt is the slow filling of the "environment" (the vitreous, lens, and other tissues posterior to the ciliary body). It will be seen from the Figure that the rates of the slow process correspond to a half-life ($t_{1/2}$) of 100 minutes for thiocyanate and of 180 minutes for sodium.

In the absence of an experimental method of determining directly values for $C_{Rm.}$, the following reasoning has been used to obtain a first approximation. The slowness of the filling of the posterior chamber is considered to be due to the slowness with which the relatively large volume of the environment is filled; hence, the apparent rate of filling of the lumped environment is characterized by approximately the same time constant as that which characterizes the slow phase of the filling of the posterior chamber.

Actually, the fact that the curves of Figure 1 become approximately straight lines for the greater values of time indicates that a single exponential describes the process with sufficient accuracy. Accordingly, the concentration $C_{Rm.}$ for various times was computed by assuming that $C_{Rm.}$ equals zero at $t = 0$ and approaches steady state in a simple exponential manner.

$$\frac{dC_{Rm.}}{dt} = k'_{diff.\,post.\,Rm.}(C_{Aq.\,post.} - C_{Rm.}) \qquad (4)$$

where

$k'_{diff.\,post.\,Rm.}$ is the coefficient of transfer for the filling of the lumped environment.

The coefficient for thiocyanate is 0.0069 and that for sodium is 0.00384.

The values for the coefficients employed in performing the numerical integration of Equations *2* and *3* were selected on the basis of the following reasoning: The volume of the posterior chamber is about one-fifth that of the anterior chamber [22]; hence K_{Flow} should be five times as great as the k_{Flow} used in Equation 1. Later it will be shown that k_{Flow} is approximately 0.017; thus, the value employed for K_{Flow} is 0.085. The value for $k_{diff.\,post.}$ (as used for thiocyanate) was fixed on the basis that at steady state $\frac{C_{Aq.\,post.}}{C_{Pl.}} = \frac{k_{diff.\,post.}}{K_{Flow} + k_{diff.\,post.}}$. For thiocyanate, which has a steady-state value of 0.61, $k_{diff.\,post.}$ must be about 0.135. Since the volume of the environment is not known, the value for $k_{diff.\,post.\,Rm.}$ was determined by obtaining a fit to the data (Figs. *2* and *3*).† Actually, this empirical method of obtaining a value for $k_{diff.\,post.\,Rm.}$ was used only for thiocyanate because the coefficient for sodium must be but 1/1.8 that for thiocyanate, since the ratio of the values of $k'_{diff.\,post.\,Rm.}$ for these ions is as 1 to 1.8.

It is possible to obtain a different value for $k_{diff.\,post.\,Rm.}$ by obtaining a fit for the thiocyanate data based on the secretion hypothesis (Equation *2*). If, now, this value (divided, of course, by 1.8) is then used as a coefficient in performing a numerical integration for sodium data, the curve so obtained will not fit the experimental points. Thus a more complex hypothesis (than secretion) would be required to explain the mode of entrance of sodium into the posterior chamber. In a subsequent paper the effect of using different values for $k_{diff.\,post.\,Rm.}$ on the curves will be treated at greater length.

RESULTS

The concentrations of thiocyanate in the posterior and anterior chambers of 184 eyes, relative to that reached in the plasma when essentially constant concentration had been attained, are shown in Table 1, Part A, for various times after intraperitoneal injection.‡

The numerical values shown in Part B of Table 1 refer to six additional eyes for which the intervals following injection were sufficiently long that the ratios of concentration

† The value for $k_{diff.\,post.\,Rm.}$ will differ from that of $k'_{diff.\,post.\,Rm.}$ because, as with small k_{Flow} and large K_{Flow}, the effect on the concentrations of the substance in any particular chamber will vary inversely with the volumes involved. The relationship in this instance is:

$$V'_{Rm.}k'_{diff.\,post.\,Rm.} = V'_{post.}k_{diff.\,post.\,Rm.} \qquad (5)$$

‡ The concentration of test substances in the plasma at time intervals less than 20 minutes varies considerably from animal to animal, so that the relative aqueous concentrations at times less than 20 minutes are known with less certainty than those representing larger time intervals.

TABLE 1.—*Concentration of Thiocyanate in Anterior and Posterior Chamber Aqueous Humor Relative to Plasma at Various Times After Intraperitoneal Injection*

Time, Min.	Concentration Relative to Plasma, %		Time, Min.	Concentration Relative to Plasma, %		Time, Min.	Concentration Relative to Plasma, %	
	Post. Aq.	Ant. Aq.		Post. Aq.	Ant. Aq.		Post. Aq.	Ant. Aq.
				Part A: Rates				
9	27	14	82	25	42	196	..	71
11	30	12	82	..	48	196	45	59
12	26	11	83	36	55	197	65	59
15	40	12	84	40	55	200	40	56
16	30	15	86	44	63	200	48	58
18	16	9	86	70	55	202	41	68
19	34	..	86	46	54	204	41	52
20	16	11	87	33	43	206	50	67
20	..	20	89	24	47	210	42	47
22	26	16	89	59	62	211	34	50
22	40	27	89	41	63	216	43	52
23	40	16	89	54	65	217	41	63
25	10	9	90	43	56	218	40	53
25	43	23	90	60	..	218	37	44
27	46	26	90	56	71	220	50	51
28	..	18	90	..	36	220	43	58
30	30	23	93	53	51	222	41	53
30	26	12	94	42	38	222	56	72
32	52	38	94	..	43	224	54	72
33	25	17	99	48	62	224	53	57
37	42	42	100	..	64	226	57	57
37	39	26	100	..	75	254	52	61
38	45	31	101	45	55	260	67	65
38	57	39	101	46	55	325	..	65
39	54	39	101	37	48	335	71	81
40	24	31	101	..	56	335	58	72
40	15	32	102	50	..	335	59	68
40	45	24	102	..	53	336	74	81
45	34	25	102	53	55	340	58	66
48	36	24	102	..	60	343	..	65
50	65	41	103	40	46	345	67	73
50	44	48	103	65	66	349	69	75
51	45	68	103	34	40	380	89	92
52	43	58	103	46	..	380	76	91
54	22	22	104	36	43	382	54	72
54	43	50	105	28	57	382	61	79
55	33	40	106	45	62	384	65	79
58	63	45	107	39	45	384	59	83
58	36	28	108	..	56	386	87	86
59	50	61	120	46	63	386	88	91
60	36	43	123	43	71	388	57	78
60	37	57	127	42	56	388	53	78
60	54	52	138	78	71	390	52	80
60	61	57	150	45	..	390	53	84
60	52	38	151	50	71	392	65	80
60	31	34	151	41	57	392	66	78
60	37	58	151	52	71	420	44	73
61	43	35	152	52	70	420	49	67
61	49	37	152	61	69	426	74	80
62	70	67	164	52	61	428	67	80
64	35	29	165	62	67	428	43	64
66	28	30	166	74	66	432	74	77
66	24	34	167	49	68	432	53	53
67	45	38	182	44	55	434	48	58
70	44	52	182	38	50	436	80	77
71	22	32	186	32	69	436	48	58
71	23	45	186	40	69	436	..	61
73	43	46	187	44	64	438	59	67
73	..	42	188	52	63	438	48	55
80	26	44	190	38	46	440	55	64
81	47	41	192	48	58	....	..	..
82	39	51	194	49	57	....	..	..
				Part B: Steady State—Repeated Injections				
1,140	55	64	1,140	75	83			
1,140	49	57	1,140	59	75	....	..	..
1,140	74	79	1,140	56	81	....	..	..
			Average	61	74	....	..	..
						....	..	..

TABLE 2.—*Concentrations of Na^{24} in Anterior and Posterior Chamber Aqueous Humor Relative to Plasma at Various Times After Intraperitoneal Injection*

Time, Min.	Concentration Relative to Plasma, %		Time, Min.	Concentration Relative to Plasma, %		Time, Min.	Concentration Relative to Plasma, %	
	Post. Aq.	Ant. Aq.		Post. Aq.	Ant. Aq.		Post. Aq.	Ant. Aq.
7	19	6	74	..	43	255	64	90
7	20	2	77	58	38	256	77	88
11	20	4	78	..	63	257	73	84
11	10	3	79	57	45	258	83	91
14	15	17	80	57	65	260	67	82
15	30	10	82	62	67	274	80	91
21	40	14	82	49	58	274	80	93
21	30	15	85	76	75	275	91	97
22	30	15	85	56	60	280	88	88
22	48	10	101	70	80	287	84	102
22	44	19	101	54	72	287	93	99
24	..	20	101	63	73	288	77	84
25	25	20	101	59	56	292	80	97
27	49	29	103	62	55	294	87	98
29	52	26	105	55	52	302	76	86
29	44	20	106	64	62	304	80	79
30	44	32	106	56	52	306	76	87
38	..	52	107	63	65	308	81	86
38	..	46	107	76	84	308	81	86
40	53	36	123	66	75	333	79	93
42	62	44	125	69	78	338	76	92
42	53	26	127	66	83	340	81	90
42	45	..	128	68	85	343	77	89
43	49	33	137	..	84	367	88	85
43	46	39	138	72	77	369	87	92
45	34	38	138	72	84	375	93	95
45	40	27	150	64	81	377	98	90
45	50	34	152	64	73	378	82	..
48	66	50	154	71	80	381	82	88
48	52	50	155	71	87	387	88	97
52	64	59	156	73	73	384	93	89
54	58	56	159	70	77	1,050	95	95
54	49	51	169	68	81	1,080	86	93
54	59	50	182	73	79	1,200	87	99
55	68	58	184	73	81	1,205	90	96
56	57	47	185	71	77	1,275	98	98
56	61	42	187	70	80	1,300	95	99
56	61	47	205	63	71	1,300	94	96
58	55	40	207	76	70	1,410	96	97
58	..	50	227	71	78	1,410	96	98
60	58	46	232	69	82	1,425	94	93
60	64	72	233	65	80	1,425	96	97
62	52	50	235	74	88	1,500	89	93
62	59	64	243	75	78	1,545	82	87
64	52	49	245	72	84	1,550	83	92
69	67	71	247	74	89	1,560	89	94
69	69	67	248	80	89	1,570	91	94
72	44	84	252	76	90	1,590	100	105
72	58	44	253	80	88	1,590	97	102
74	50	59	254	81	87	...	..	..

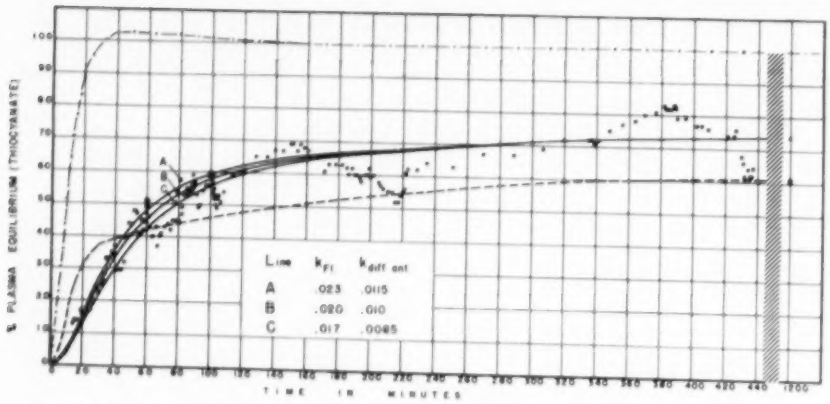

Fig. 2.—Relative concentrations of thiocyanate in the plasma and anterior and posterior chamber aqueous humors, where the concentration in the plasma once the level had become essentially constant was arbitrarily set at 100%. The dot-dash line represents the concentration in the plasma. The solid lines represent numerical integrations of the data for anterior chamber aqueous humor, using the values for the coefficients of transfer as indicated on the graph. The broken line represents the concentration of thiocyanate in the posterior chamber aqueous humor.

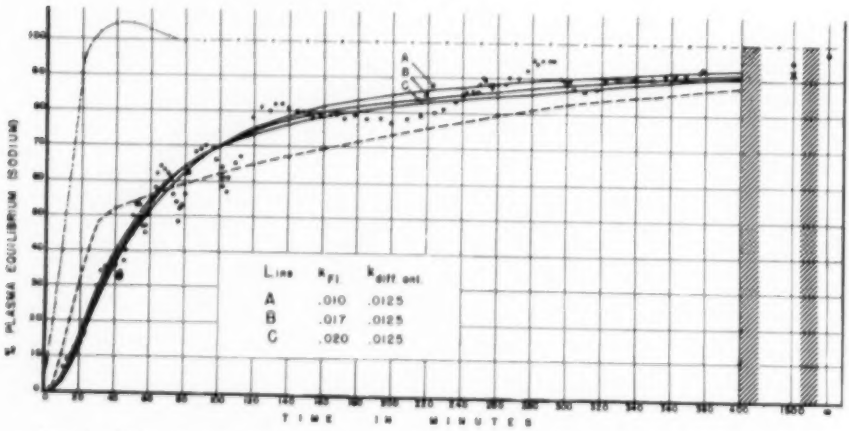

Fig. 3.—Relative concentrations of sodium in the plasma and anterior and posterior chamber aqueous humors, where the concentration in the plasma once the level had become essentially constant was arbitrarily set at 100%. The dot-dash line represents the concentration in the plasma. The solid lines represent numerical integrations of the data for anterior chamber aqueous humor, using the values for the coefficients of transfer as indicated on the graph. The broken line represents the concentration of sodium in the posterior chamber aqueous humor.

substantially represent steady-state conditions. The average steady-state ratio $\frac{C_{Aq.post.}}{C_{Pl.}}$ is 0.61 and the ratio $\frac{C_{Aq.ant.}}{C_{Pl.}}$ is 0.74.

Table 2 consists of analogous data for Na^{24}. However, in the instance of sodium a more reliable estimate of steady-state ratios can be obtained by chemical analysis than by use of isotopes, since it is a constituent normally present in the aqueous humor. Results of experiments of this kind were presented in previous papers, where it was stated that the steady-state ratio of sodium in the anterior chamber aqueous humor was 0.97 [19] and in the posterior chamber 0.98 [24] that of plasma.

The curves presented in Figure 2 show the relative concentrations of thiocyanate in the plasma, anterior chamber aqueous humor,

and posterior chamber aqueous humor. The curves for the plasma (dot-dash line) and posterior chamber aqueous humor (line of dashes) are based on sliding averages of the data, but to avoid unnecessary complication of the chart, the points are not shown. The points shown represent sliding averages of the data for the anterior chamber aqueous humor. The three solid lines represent curves resulting from numerical integration (based on Equation 1), with use of the values shown on the chart for the coefficients of transfer, and the average value of the concentration in the posterior chamber aqueous humor at each time, as read from the curve representing posterior chamber aqueous humor data. The middle curve (*B*) would seem to provide the best fit to the data, the coefficients of transfer being k_{flow}=0.020 and $k_{diff\ ant}$=0.010.

Figure 3 shows similar data for sodium. As in the graph for thiocyanate, the middle curve is believed to represent the best fit to the data. In the case of sodium, the slope of the curve is much more sensitive to changes in $k_{diff\ ant}$ than in k_{flow}, the reason being that the difference $C_{Pl.}-C_{Aq.post.}$ is much greater than the difference $C_{Aq.ant.}-C_{Aq.post.}$ during the first period of the experiment. The various curves drawn on the basis of different values for $k_{diff\ ant.}$ are omitted, however, in order to avoid unnecessary complication of the chart. The coefficients used in obtaining the middle line are k_{flow}=0.017 and $k_{diff\ ant.}$=0.0125. Taking both substances into consideration, it appears that the coefficient of flow into, and therefore flow out of, the eye lies between 0.017 and 0.020.

The data shown in Figure 4 represent sliding averages of the concentrations of sodium (open circles) and thiocyanate (filled circles) in the posterior chamber aqueous humor at different times following injection. The steady-state value for sodium (0.98) is based on chemical analysis, and the value is taken from an earlier paper, as indicated previously.

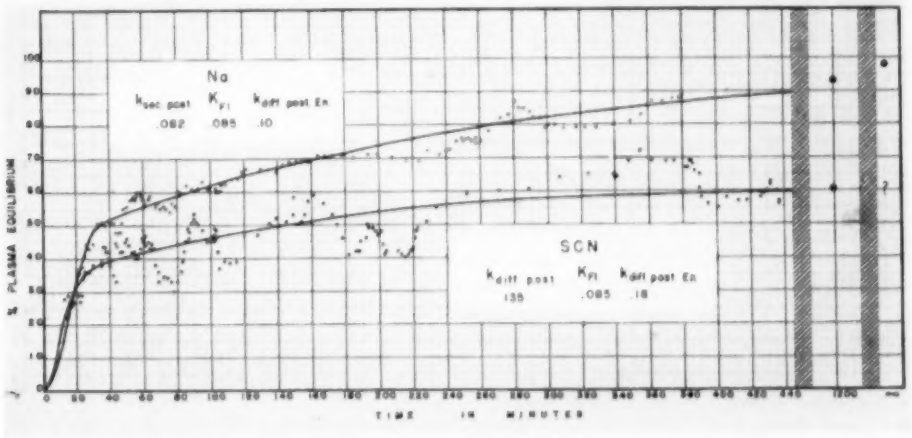

Fig. 4.—Concentration of sodium (open circles) and thiocyanate (filled circles) in the posterior chamber aqueous humor relative to that in the plasma at various times after intraperitoneal injection. The solid lines represent numerical integration based on the secretory hypothesis (sodium) and diffusional hypothesis (thiocyanate). The coefficients for the diffusional exchange with the environment are calculated under the same assumptions in the two solid curves.

The upper solid line represents a numerical integration based on the hypothesis that sodium enters the posterior chamber according to the "secretion" process described in Equation 2, and the lower solid line represents a similar numerical integration based on the hypothesis that thiocyanate enters

according to the diffusion process described by Equation 3. The values for the coefficients are indicated directly on the charts. It is apparent that the theoretical curves are consistent with the data.

It is possible to arrive at different values for $k_{diff.post.Ep.}$ as mentioned earlier under "Mathematical Considerations." However, these values, when employed in performing a numerical integration, give rise to curves which will fit the experimental data for only one ion or the other. It is not possible to arrive at a value for the coefficient which will fit the data for both thiocyanate and sodium on the assumption that both ions enter the posterior chamber by either diffusion or secretion only. The use of values for $k_{diff.post.Ep.}$ other than the one employed would require an hypothesis more complex, postulating a dual mode of entrance for a single ion. This subject will, as stated earlier, be discussed in greater detail in a subsequent paper.

Values for $k_{diff.ant.}$ can be computed for any substance (Equation 1c) from a knowledge of the flow rate and the concentrations of the substance in the posterior and anterior chamber aqueous humors relative to those in the plasma under steady-state conditions. Table 3 shows the results of such computations for a number of constituents of the aqueous humor, in comparison with those for sodium and thiocyanate. For the purpose of computation, the value selected for k_{flow} was 0.017. The values for the steady-state concentrations were taken from a previous paper.[3] Although the appropriate information concerning the concentrations is available for lactate and glucose, no computations were made for these substances, because production and utilization, respectively, by the lens and cornea would give rise to relatively large errors. It is apparent that different values for $k_{diff.ant.}$ would result were a different value for k_{flow} employed, but the relative order of diffusibility of the different substances would remain the same.

From the computed values of $k_{diff.ant.}$ and a knowledge of the steady-state concentration

TABLE 3.—*Coefficient of Diffusion* from Blood to Anterior Chamber for Various Constituents of Aqueous Humor*

Substance	Coefficient of Transfer by Diffusion †	Per Cent of Total Amount of Substance Entering Anterior Chamber by Diffusion ‡
Chloride	0.013	46
Bicarbonate	0.033	58
Ascorbate	0.006	0.5
Phosphate	0.011	66
Thiocyanate	0.016	49
Sodium	0.0125	43
Urea	0.009	30

* The coefficients are calculated neglecting the effect of exchange with the cornea and lens. The magnitude of the errors so introduced is not readily determinable and must vary from substance to substance.

† $k_{diff.ant.}$

‡ That is, the per cent of the total amount of each substance which enters the anterior chamber by diffusion from the blood, presumably across the iris vessels. (The difference in amount between the per cent shown and 100% enters the anterior chamber by flow from the posterior chamber.)

in the posterior chamber, it is possible on the basis of Equation 1 to compute for any substance the fraction of the total amount of this substance which enters the anterior chamber by one process or the other. A purely schematic diagram illustrating the two modes of entrance of a substance is shown in Figure 5, where the numerical data used for illustration represent the relative concentrations of thiocyanate. Since (from Equation 1) $k_{flow}C_{Aq.post.}+k_{diff.ant.}C_{Pl.}$ represents the total amount of the substance entering the anterior chamber, simple substitution of numerical values in the equation makes it possible to compute the fraction entering the anterior chamber by either means. The per-

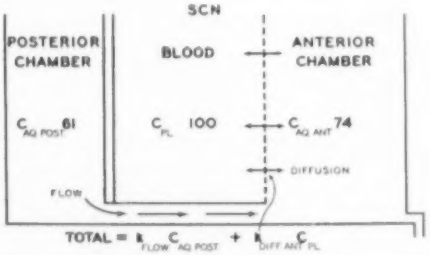

Fig. 5.—Schematic representation of the two means of entrance of substances into the anterior chamber.

centage of the total amount of each substance which enters the anterior chamber by diffusion is also shown in Table 3.

COMMENT

The present investigation has dealt with the following three aspects of the problem of aqueous humor dynamics: (1) the portion of the total amount of several anions, the cation sodium, and the nonelectrolyte urea in the anterior chamber which enters by flow from the posterior chamber and that which enters by diffusion directly from the blood; (2) the rate of flow of aqueous humor, and (3) the possible mechanism of entrance of anions and cations into the posterior chamber.

Concerning the first aspect, the results support the idea that both the negatively charged ion, thiocyanate, and the positively charged ion, sodium, enter the anterior chamber both from the posterior chamber and directly from the blood, the mechanisms involved presumably being flow and diffusion, respectively. From a qualitative point of view, this is made evident in both cases from the crossing over of the curves representing rate of accumulation in the posterior and anterior chambers (Figs. 2 and 3). It is evident that were all of the test substance to enter from the posterior chamber, its concentration in the anterior chamber could never exceed that in the posterior chamber. In fact, the slope of the line representing the rate of accumulation in the anterior chamber at the time that the crossing over occurs is a measure of the coefficient of diffusion ($k_{diff\,ant.}$) into the anterior chamber, since the amount of the test substance flowing into and out of the anterior chamber per unit time is equal.

From a quantitative point of view the availability of data concerning the rate of accumulation of thiocyanate and sodium in both the posterior and the anterior chamber aqueous humor has made it possible to obtain a numerical evaluation of the contribution by the two means of entrance.

Since substances do seem to gain entrance to the anterior chamber by at least two routes, theoretical curves based on an assumption to this effect fit the data substantially better than curves based on the simpler assumption of a single mode of entrance. The factor limiting the accuracy of fit of the curves to the data now apparently has become the individual variation in the animals, experimental errors incident upon the methods employed, etc., rather than the simplifying assumptions used in formulating the present hypothesis.

It may be recalled that a reasonably good fit to the data, representing the rates of accumulation of both thiocyanate and sodium, was given by ya flow rate in the range of 1.7% to 2.0% per minute. Thus, a flow rate having a value of approximately 1.7% per minute would seem to be a reasonable estimate of the rate of flow as found in all the experiments described. However, it should be recalled that the method of calculating k_{flow} used in this paper involves the assumption that the rate of flow into the anterior chamber from the posterior chamber and the rate of flow out of the anterior chamber are identical. To the extent that this assumption may be wrong, the true value for k_{flow} out may be different from 1.7% per minute.

The value of 1.7% per minute for flow rate is substantially in excess of those reported by the majority of previous investigators, including that, namely, 1.1% per minute, found by Kinsey and Bárány,[9] who used paraaminohippuric acid and two other test substances which have the property of being rapidly removed from the blood by excretion by the kidney. Some of the shortcomings of the original paraaminohippuric acid method, notably its dependence upon the assumption that both eyes behave in an identical manner, and the use of a correction factor embodying information derived from a separate set of experiments, have been discussed recently by Bárány and Wirth.[23] However, the results obtained by these authors, using an improved method for estimating rate of outflow in individual animals,

led to a similar value. The possibility should be investigated, however, that the paraaminohippuric acid itself might influence the flow rate. It is beyond the scope of the present paper to attempt to bring into agreement the paraaminohippuric acid results and those reported here, if indeed the differences are real; further experimentation will be required to resolve any differences in the flow rate as obtained by the two methods.

Another discrepancy between the present results and those reported by previous authors is the difference between the values for the turnover rates (k_{out}) in the anterior chamber. The present study gives rise to k_{out} values of about 0.03 for both sodium and thiocyanate, while values previously cited are considerably lower, ranging mostly between 0.010 and 0.015. For example, Kinsey and co-workers § reported values of 0.014 to 0.016 for a series of ions, including sodium and thiocyanate; Kinsey and Bárány [9] reported 0.011 for sodium, and 0.012 to 0.014 for paraaminohippuric acid, Rayopake, and Diodrast. Palm [10] reported a value of approximately 0.01 for both sodium and phosphate. In computing the turnover rates, Kinsey and Bárány placed emphasis on periods in excess of 40 minutes. It is apparent now that the turnover rate so determined was too low because of the effect on the curve of diffusion into vitreous, lens, etc. It should be mentioned, however, that in their recent publication Davson and Matchett [11] argue that the parameter k_{in} should preferably be deduced from the rate at which steady state is approached, i. e., from the later stages of the process rather than from its initial stage.

The effect of the time required to fill the spaces surrounding the posterior chamber is manifested in still another way. Kinsey and Bárány assumed that the steady-state ratio for the anterior chamber aqueous humor for sodium was 0.93. This value was based on determination of the distribution of sodium 13 hours after intraperitoneal injection. In the present experiments the average distribution ratio is 0.96 for the last 18 eyes shown in Table 2 for the anterior chamber (average time, approximately 24 hours). The value for steady state as determined chemically, however, is more nearly 0.98. The rate of filling of the anterior chamber at time periods in excess of five hours can be calculated graphically in the usual manner by plotting the logarithm of the difference between the observed value and that at steady state against time. The data can be represented by a straight line, the slope of which corresponds to a rate of filling corresponding to a half-life of 10 hours. On the assumption that the rate of filling is not altered appreciably at times in excess of 24 hours, one can compute on this basis that 4.3 hours must elapse before the concentration of sodium in the anterior chamber attains a value within 0.5% of the steady-state concentration. These observations may help to explain differences in reported values for the steady-state distribution ratio of sodium. They are in good agreement with observations reported by Maurice [20] that the distribution ratio continues to increase long after the time expected on the basis of the simple equations generally used.

The values for the relative concentration in the anterior and posterior chambers taken at times before the plasma concentration attains an approximately constant value (approximately 20 minutes) are lower than they would be had the concentration in the plasma been at constant level from the start.

This introduces no difficulty in fitting the theoretical curves to the data, since the actual plasma concentration at these early times was used in making the numerical integrations.

Concerning the third question, i. e., the mode of entrance of anions and cations from the ciliary body into the posterior chamber, the experimental data for sodium are found to fit an equation derived from a secretory hypothesis, whereas the experimental data for thiocyanate fit an equation derived from a diffusion hypothesis. When an attempt is made to fit the data for the two ions to the respective opposite hypothesis, the discrepancy between the experimental and the theoretical values far exceeds the experimental

§ References 5 and 25.

variations involved. This is evidence that the two ions are treated differently by the mechanisms bringing them into the posterior chamber. Whether or not these mechanisms are actually those envisaged in setting up the equations, or other mechanisms involving different physiologic implications, remains an open question.

SUMMARY

Measurements were made of the rate of accumulation of two test substances (sodium and thiocyanate) in the posterior and anterior chambers of the rabbit eye. Applying an elaboration of a theory of aqueous humor dynamics to these determinations, the coefficients of transfer into the anterior chamber by flow from the posterior chamber and by diffusion through the iris vessels are estimated.

The rate of flow out of the anterior chamber ascertained in this manner would appear to lie between 0.017 and 0.020, i. e., between 1.7% and 2% per minute of the volume of the anterior chamber. The diffusion rates in corresponding units for thiocyanate and sodium, respectively, are approximately 0.010 and 0.0125. The fraction of the amount of the test substances which enters the anterior chamber by the two modes of entrance is computed from coefficients of transfer and data concerning the concentrations in the posterior chamber under steady-state conditions. About half of the thiocyanate and slightly less (43%) of the sodium were found to enter the anterior chamber by diffusion, the remainder in each instance entering by flow from the posterior chamber. Similar computations were made for urea and for a number of negatively charged constituents of the aqueous humor, and it was found that, except for ascorbate and urea, of which 99% and 70%, respectively, enter by flow, approximately half the total amount of each ion enters by diffusion and half by flow.

The data for the entrance of sodium to the posterior chamber were found to fit a curve derived from a secretory hypothesis concerning the mode of entrance, whereas those for thiocyanate were found to fit a curve derived from a diffusion hypothesis. Although these findings do not demonstrate the exact nature of the transport mechanisms involved, it is believed that they justify the conclusion that the mechanism for the two ions are different.

Dr. Elek J. Ludvigh, Dr. Jonas S. Friedenwald, and Dr. Ernst Bárány gave many helpful suggestions and criticisms, and the Misses Eileen Horgan and June Twomey, Mrs. Barbara Zolliker, and Dr. Enriqueta Camacho gave technical assistance.

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Treatment of Pseudomonas Corneal Ulcers

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Corneal ulcers due to Pseudomonas aeruginosa are usually central and extremely destructive. In the majority of instances the course of an untreated Pseudomonas ulcer is one of widespread corneal suppuration, necrosis, and perforation within a few days. Treatment of these ulcers has not often resulted in useful vision. It is well to remember, however, that P. aeruginosa is in some instances a saprophyte which possesses little or no virulence in the eye or in other parts of the body. This has been demonstrated by the experimental production in animals of Pseudomonas corneal ulcers which have a relatively benign course even when untreated. Fulminating corneal ulcers, however, can be produced experimentally by the use of virulent strains. This variation in degree of virulence must be kept in mind when the success of various forms of therapy is being evaluated.

Prior to the advent of polymyxin, it was assumed that the poor results of therapy were due to the high innate resistance of the Pseudomonas organism to antibiotics and chemotherapeutic agents. Wiggins [1] demonstrated that polymyxin B is a much more effective antibiotic agent against P. aeruginosa than is chlortetracycline (Aureomycin) or streptomycin. He also demonstrated the prompt arrest and satisfactory cure of Pseudomonas corneal ulcers when topical polymyxin B therapy was instituted 6, 12, and 18 hours after inoculation of the rabbit cornea with organisms.

In determining the concentration of polymyxin B in the normal rabbit eye following topical instillations, corneal baths, and subconjunctival injection, Wiggins found that there was no appreciable penetration into corneal stroma or aqueous except by subconjunctival injection. Similar determinations performed on eyes with abraded epithelium indicated good penetration into corneal stroma by all three of the above-mentioned methods of administration, particularly by corneal baths. There was no significant penetration into the vitreous. Data for the penetration of parenterally administered polymyxin B are not available, but Ainslie and Smith [2] have shown that this method of administration of polymyxin E gives no significant penetration into the rabbit eye.

The purpose of the present article is to review the cases which have been reported both before and after the advent of polymyxin and to add two cases treated systemically with polymyxin B.

In 1922 Morelli [3] reviewed 38 cases in the literature and reported loss of the eye in 23, leucoma in 14, and a nebula in 1.

There have been 58 cases reported since 1922 for which adequate data are available. Of the 24 cases treated prior to the sulfonamide and antibiotic era (1939), 12 eyes were either eviscerated or enucleated,* 9 eyes retained a visual acuity of 6/60 or less,† and only 3 eyes retained a visual acuity of better than 6/60.[11] Of the 25 cases treated subsequent to 1939 with sulfonamides or antibiotics other than polymyxin, 10 eyes were either enucleated or eviscerated,‡ 9 eyes retained a visual acuity of 6/60 or less, § and 6 eyes retained a visual acuity of better than 6/60. ‖

* References 4 through 10.

† References 6 and 11 through 13.

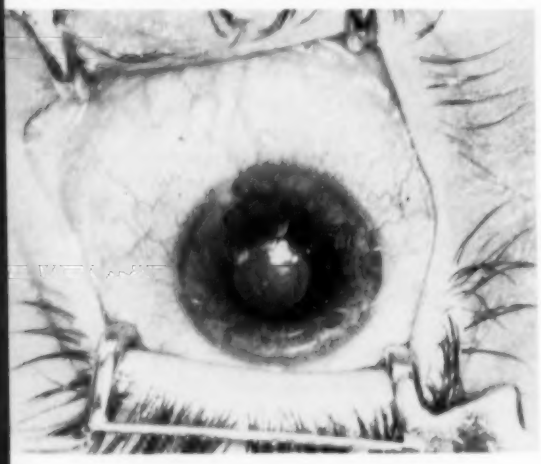
‡ References 10 and 14 through 16.

§ References 10 and 15 through 20.

‖ References 10, 16, and 21.

Fig. 1 (Case 1).—Appearance on April 2, 1952, before polymyxin therapy.

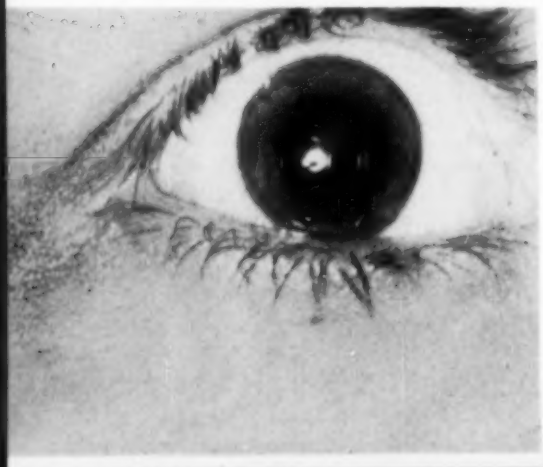
Fig. 2 (Case 1).—Seventh day of treatment.



Of the nine cases which have been treated topically or subconjunctivally with polymyxin B or polymyxin E, one eye was eviscerated,[22] seven eyes retained a visual acuity of 6/60 or less, ¶ and only one eye retained a visual acuity of 6/24.[22] Wiggins [26] reported three additional cases which were treated topically with 0.1% to 0.5% polymyxin B every hour but did not record the final visual acuity. It is evident that the results in the polymyxin-treated cases are not as satisfactory as might be anticipated from the in vitro findings.

¶ References 22 through 25.

Fig. 3 (Case 1).—Appearance Aug. 13, 1953.



Two cases of Pseudomonas corneal ulcer were treated by topical and parenteral polymyxin B at the U. S. Naval Hospital, Philadelphia.

Case 1.—K. W. G., a 25-year-old man, was admitted to the U. S. Naval Hospital at Philadelphia on April 1, 1953, with the chief complaint of pain and blurred vision in the right eye of four days' duration. Four days prior to admission he noted the sensation of a foreign body in the right eye. On the day before admission a small superficial foreign body was removed from the apex of of the cornea. The eye was slightly injected, according to the report of the examining physician.

During the ensuing 24 hours a central corneal ulcer developed at the site of removal of the foreign body, although the patient had been placed on treatment with 0.25% chloramphenicol (Chloromycetin) drops every two hours. Before admission the eye became redder and more painful, and vision was increasingly blurred.

Physical examination on admission was negative except for the ocular findings:

V. O. D.: Finger counting at 5 ft. (1.5 meters)
V. O. S.: 6/6

The right eye showed severe photophobia, lacrimation, and marked ciliary and conjunctival injection. A corneal ulcer 3 mm. in diameter, which stained with fluorescein, was noted at the apex of the cornea. There was a small amount of purulent exudate within the conjunctival sac. Biomicroscopic examination revealed not only denuding of the epithelium and destruction of Bowman's membrane, but an infiltration of the stroma, which extended over a somewhat wider area than that of the ulcer. This infiltrated area extended to Descemet's zone and was barely translucent. The anterior chamber contained many cells, and a dense flare was present. The fundus could not be visualized owing to the corneal ulcer and the turbidity of the anterior chamber. Tactile tension was normal. The left eye was essentially normal.

Material for culture was immediately taken and sensitivity tests ordered, since a resistant organism was suspected. In the meantime the patient was placed on treatment with 600,000 units of procaine penicillin G immediately and 300,000 units every

six hours. Chloramphenicol drops, 0.5%, were instilled into the right eye every hour. Within six hours the report was that of P. aeruginosa not sensitive to any of the following drugs.

Drug	Amount/Disc
Dihydrostreptomycin	1 γ
Penicillin	0.5 unit
Oxytetracycline (Terramycin)	10 γ
Chloramphenicol	10 γ
Chlortetracycline	10 γ
Erythromycin	0.5 γ
Polymyxin B	0.5 γ
Bacitracin	2 units

Sensitivity tests were immediately repeated, using a greater concentration of the same drugs. On the morning of the second hospital day it was evident that the eye was worse, both subjectively and objectively (Fig. 1). The ulcer had enlarged moderately, and the infiltration area had become larger and opaque. The anterior chamber contained a great increase in cells and protein aggregates, and there was a heavy deposit of cells and fibrin in the dependent portion of the anterior chamber. An hypopyon was evident grossly. Report of the second sensitivity test at this time was as follows:

Drug	Result
Polymyxin B sulfate	2 mm. zone of inhibition with 30 γ disc
Chloramphenicol	Slight inhibition with 60 γ disc
Dihydrostreptomycin	Slight inhibition with 10 γ disc
Chlortetracycline	Slight inhibition with 30 γ disc

Although the inhibition around the polymyxin disc was very small, it was sharply demarcated. Therefore, all previous medication was discontinued, and the patient was placed on treatment with polymyxin B sulfate intramuscularly, 2.5 mg. per kilogram of body weight divided into four injections daily. He was also placed on therapy with 0.2% topical polymyxin B in isotonic saline every hour, 1% atropine three times daily, and hot compresses every hour. Within 10 hours the patient had a gratifying diminution in the amount of pain in the eye. Within 20 hours the gross evidence of hypopyon had disappeared and the stromal infiltration showed clearing. There were still many cells and a heavy aqueous flare in the anterior chamber.

By the fifth day of treatment there was no staining of the ulcer. The area of infiltrate had become translucent everywhere except in the direct center. The aqueous flare was 1+ to 2+, with marked diminution in the number of cells in the anterior chamber. By the seventh day the entire chamber was clear except for an occasional cell (Fig. 2). At this time the infiltrated area extended only into superficial stroma. Both topical and parenteral polymyxin was discontinued.

The eye, which was still rather red, became much whiter and less congested several days after local polymyxin was discontinued. Improvement continued until the time of discharge, on the 19th hospital day, after which he was observed as an outpatient. Visual acuity in the affected eye at this time was 6/60, not corrected with pinhole. A picture taken on Aug. 13, 1953, reveals a marked decrease in the density of the scar (Fig. 3). On the last examination, Jan. 8, 1954, nine months after this episode, he had a 3 mm. macula involving the superficial stroma, associated with moderate thinning of the

Fig. 4 (Case 2).—Before polymyxin therapy.

Fig. 5 (Case 2).—Seventh day of therapy.

Fig. 6 (Case 2).—Three months after treatment.

stroma at the apex. Vision with cycloplegic refraction was as follows:

O. D.: +4.25 sph ⌒ —0.50 cyl ax 40 = 6/9 —2
O. S.: +1.00 sph ⌒ —0.50 cyl ax 180 = 6/5

There were no side-reactions except for paresthesias of the face and scalp, which began on the third day of therapy and persisted throughout the treatment. No evidence of nephrotoxicity was indicated by daily urinalysis. Two blood urea nitrogen determinations and blood cell counts showed no abnormality.

Case 2.—P. A., a 47-year-old man, had a superficial metallic foreign body removed from the upper nasal paracentral portion of the right cornea on Oct. 30, 1953. An antibiotic solution was instilled, and the eye was patched for several hours. Two days later, after experiencing discomfort in the eye, he was admitted to the hospital with a small corneal ulcer and secondary iritis.

The initial hospital examination of the right eye revealed a visual acuity of 6/12, corrected to 6/9 with pinhole. There was a small, clear, staining area in the upper paracentral area nasally, which was surrounded by a minimal gray, superficial infiltrate. Moderate circumcorneal injection was present, and there were numerous cells and a moderately dense flare in the anterior chamber. The remainder of the examination, including that of the left eye, was normal. Material for culture was taken, and the patient was placed on topical instillations of 0.25% chloramphenicol every hour and 2% atropine twice daily, with warm compresses to the right eye. Within 24 hours the ulcer was markedly worse, the stromal infiltrate being greatly increased in density, diameter, and depth. Cells and flare in the anterior chamber were very dense, and there were large folds in Descemet's membrane (Fig. 4). Visual acuity in this (right) eye diminished to 6/24, corrected to 6/20 with pinhole. A 24-hour culture revealed P. aeruginosa, which responded to the antibiotic sensitivity tests as follows:

Drug	Amount/Disc	Reaction
Dihydrostreptomycin	1 γ	None
Penicillin	0.5 unit	None
Oxytetracycline	10 γ	None
Chloramphenicol	10 γ	1+
Chlortetracycline	10 γ	1+
Polymyxin	0.5 γ	3+
Bacitracin	2 units	None

All previous medication was discontinued, and the patient was immediately placed on treatment with polymyxin B sulfate intramuscularly, 2.5 mg. per kilogram of body weight divided in four doses daily, and with a 0.1% solution topically every hour, in addition to atropine 2% topically twice daily. Within 48 hours the ulcer was definitely, but not dramatically, improved. On the next day, the third day of polymyxin therapy, the patient developed moderately severe ataxia and paresthesias of the face and scalp, so that the intramuscular dose of polymyxin was halved. A culture of the ulcer taken on the same day revealed hemolytic and nonhemolytic Staphylococcus aureus organisms, which were very sensitive to chloramphenicol, oxytetracycline, and chlortetracycline. The patient was placed on chloramphenicol, 0.25% given topically every hour, in addition to the polymyxin. Two days later, on the fifth day of polymyxin therapy, the ulcer did not seem to show further improvement; therefore 0.5% oxytetracycline drops were substituted for the topical chloramphenicol, and the patient was started on chloramphenicol therapy, 500 mg. every six hours by mouth. Two days later, on the seventh day, the ulcer was again improved. The density and diameter of the stromal infiltrate were much less than formerly, and the anterior chamber contained a dense aqueous flare with only a few cells. There was a tiny central staining area of the ulcer (Fig. 5). The polymyxin dosage was then raised to the original level. On the 11th day of polymyxin therapy the oral administration of chloramphenicol was discontinued, since the ulcer seemed to be stationary. Culture of material taken on the previous day revealed no growth. Since the ulcer still stained and the reason for failure to heal was not apparent, an injection of 40,000 units (4 mg.) of polymyxin B was given subconjunctivally after procaine infiltration analgesia had been produced. There was a tremendous conjunctival chemosis within one hour, and the patient complained of considerable pain. The chemosis finally subsided, after three days. Topical oxytetracycline and polymyxin were continued in conjunction with intramuscular polymyxin, and the ulcer finally healed, on the 17th day of polymyxin therapy. At this time there were a few cells and a slight aqueous flare in the anterior chamber. Intramuscular polymyxin was discontinued on the following day, and topical medication was discontinued six days later. Visual acuity (O. D.) at that time, on the 24th hospital day, was 6/24, corrected to 6/9—1 with pinhole.

Refraction on Feb. 10, 1953, three months later, revealed the following:

O. D.: —1.50 sph ⌒ —1.25 cyl ax 130 = 6/7.5
O. S.: +0.75 sph ⌒ —0.50 cyl ax 170 = 6/5+

Slit-lamp examination at that time revealed moderate thinning of the stroma in the affected area, and the scar appeared to be of much less density than formerly (Fig. 6). Repeated blood urea nitrogen determinations, white and red blood cell counts, and urinalyses revealed no abnormalities during treatment. There was a residual 2 mm. macula located just above and nasal to the pupillary axis.

COMMENT

From a review of the cases previously reported, it is evident that there is no marked difference between any of the methods of therapy so far as the salvaging of useful vision is concerned. Good results (a visual acuity of better than 6/60) were obtained in nine cases treated in the early stages of ulceration with agents other than polymyxin.

The encouraging results of combined topical and systemic use of polymyxin B in the present two cases should justify further use of this therapy to determine whether these results were due to the low virulence of the organism or to the early onset of therapy, or whether combined therapy is really more effective than other methods of administration of polymyxin. Systemic therapy, when employed, should be used on patients without preexisting renal damage, and the patient should be hospitalized in order that renal and neurotoxicity may be detected in the early phases. It is also suggested that secondary Gram-positive bacterial invaders should be considered when polymyxin is employed, particularly when the response is not satisfactory.

Since early treatment has been productive of the best results, regardless of the type of therapy employed, it would seem to be highly advisable to take a smear and culture from all corneal ulcers and to institute immediate specific therapy when P. aeruginosa is found or suspected clinically. Smears of the organism from the ulcer are diagnostic in many instances, and recognition of the rapid and characteristic growth on culture is also valuable. Antibiotic sensitivity tests of this rapidly growing organism can be performed in as short a time as six hours.

SUMMARY

A review of the literature since 1922 reveals 58 cases of Pseudomonas corneal ulcers for which adequate data are available. An approximately equal number of cases are omitted because of inadequate information.

An analysis of these cases shows that there has not been an increase in the number of cases in which useful visual acuity has been salvaged since the advent of topical and subconjunctival polymyxin therapy. It is suggested that a factor in these poor results has been the institution of treatment at a relatively advanced stage of ulceration.

The efficacy of treatment in the cases reviewed would seem to depend on early treatment rather than on the type of therapy employed.

Treatment with combined topical and parenteral polymyxin B sulfate therapy in two cases in the early stage of ulceration resulted in a corrected visual acuity of 6/9—2 and 6/9, respectively.

The encouraging results of combined topical and parenteral polymyxin therapy in the two cases here reported seem to justify further trial and reports of this method.

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Chorioretinal Burns Produced by Atomic Flash

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The intensity of radiant energy released at detonation of an atomic bomb in the form of infrared and visible light is extremely high. It is a physical agent with which ophthalmologists are familiar because it produces the well-known eclipse burn of the retina. It is this infrared and visible light which produces the atomic chorioretinal burns which are the subject of this presentation. This report is the first of a large-scale study of this hazard.

Eclipse blindness, with its typical macular burns, has been reported by Birch-Hirschfeld *; Verhoeff, Bell, and Walker [123]; Alexander [1]; Aubaret [3]; Lundsgaard and Rönne [82]; McCulloch [84]; Rosen [104]; Tower [120]; Zade †; Jess,‡ and many others. Excellent reviews have been published by Lauber [73]; Birch-Hirschfeld [14]; Verhoeff, Bell, and Walker,[123] and Irvine.[64]

While the components of light which produce the damage are the same for visible light and infrared radiation, there are some rather marked differences between the two. The eclipse burn is incurred through a very small pupil; hence an appreciable period of time is required to heat tissue sufficiently to damage it. During this period the vascular system of the eye can dissipate some of this heat. In the atomic burn most of the energy is delivered so rapidly as to be almost instantaneous, thus giving no opportunity for vascular dissipation and very little for dissipation by conduction. In addition, it may well be delivered through the widely dilated pupil occurring at night. This wide-open pupil will admit roughly 50 times the energy passed by the small pupil in the same period of time. So, while the physical agent is the same, there are differences which warrant careful consideration.

The extremely high intensity of radiation from the atomic flash has been recognized from the earliest tests. As a result, the eyes of practically all observers at atomic detonations have been carefully protected by very dense filters required by the test organization of the Atomic Energy Commission. These filters transmit less than 0.5% of the visible light falling on them. The literature reveals no report of such a burn, except for a single case of bilateral central scotoma incurred in the Hiroshima atomic explosion (Oyama and Sasaki §). The main reason for the paucity of burns in the Hiroshima incident is apparent—detonation in bright sunlight with pupils of the observers constricted to small size. There were other factors also, including the size of the bomb.

The study here reported was done in three parts, and it is not yet completed. Insofar as the pathological findings are concerned, this must be considered a preliminary report. In this study the physical factors involved and the effect of these factors on the eye will be considered in the first part. The second portion will give the results obtained in an experiment using 700 rabbits in six atomic detonations in Nevada in 1953. The third portion will be a brief summary of the pathological findings in these retinal burns. The use of this form of radiant energy in therapy

From the U. S. A. F. School of Aviation Medicine.

* References 12 through 15.

† References 137 through 139.

‡ References 66 through 68.

§ Oyama and Sasaki,[93] cited by Cogan and others.[29]

of several eye conditions which are presently difficult to treat by conventional surgical methods will be discussed.

I. PHYSICAL FACTORS

A theoretical consideration of the physical factors involved led to the prediction that such lesions could be produced considerably farther away from an atomic explosion than any other damage to living beings (Büttner and Rose ‖). Heat damage to living tissue depends on the temperature and the length of time the temperature persists. The increase in temperature of matter depends on the energy absorbed per unit volume. If the energy is irradiated on a surface and absorbed by a layer of known thickness and absorption, the temperature during the heating period depends on the irradiance (that is, the energy arriving per unit area and unit time, e.g., calories per square centimeter per second). There is a difference between skin damage from thermal radiation and the production of chorioretinal lesion by thermal radiation. The irradiance from an atomic fireball on a surface, e.g., on skin, depends on radiant emittance and air attenuation and on the inverse square of the distance. Owing to the image formation in the eye, the irradiance of the retina does not depend on the inverse square of the distance. It depends on the radiant emittance of the fireball, on the square of the relative opening of the optics, (pupillary radius divided by focal length), and on attenuation by the air and the ocular media. If air absorption did not occur, irradiance on the retina would not vary with distance. In the perception of brightness a similar phenomenon is well known. Owing to the constancy of illumination of the retina, a surface appears of equal brightness unless the distances are large enough to introduce effects of attenuation by the air.

The radius of the image of an atomic fireball on the retina varies linearly with the radius of the fireball and the distance from the fireball. Thus, with a pupil of given size at a given distance, a certain amount of energy is distributed over the image area. If the subject is twice as far away, the amount of energy passing through the same pupil will only be one-fourth as great; however, the image area in which the energy falls will only be one-fourth as large. The energy per unit area will therefore be constant except for the attenuations produced by air and ocular media, as mentioned above.

Most of the following discussion (but not all of the experiments later described) will be concerned with atomic bombs equivalent to 20,000 tons of TNT.[46] Such a bomb produces a fireball of 13,700 mm. 0.1 msec. after explosion. During the first second the fireball

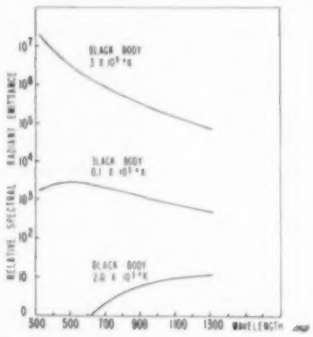


Fig. 1.—Spectral emission of black bodies of 3,000,000° K, 6,100° K, and 2,000° K, representing three phases of the atomic fireball.

grows to about 10 times this radius, and it persists for about three seconds after the explosion.

While expanding, the fireball cools rapidly. At 0.1 msec. the surface temperature is 300,000°K. After 10 msec. it is 2000°K; then it rises again, reaches a maximum of 7500°K early in the first second, and finally drops to ambient temperature at three seconds. The radiant flux per unit area and the quality of radiation change considerably with the surface temperature of the fireball. Spectral emission measurements have not been published. Figure 1 gives, therefore, spectral emission computed on the assumption of black body radiation and Planck's formula. The radiation at 0.1 msec. is high in ultra-

‖ Büttner and Rose [25]; personal communication, 1950.

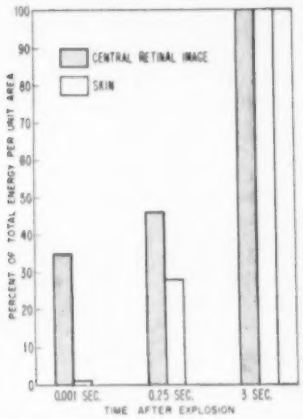


Fig. 2.—Time of incidence of certain percentages of the total thermal energy per unit area from a nominal atomic bomb for the central part of a retinal image (dark column) and the skin (white column).

violet and "blue" radiation. The radiation at 10 msec. is "reddish"; the radiation during most of the time thereafter is fairly well represented by the third curve for 6100°K.

The initial image on the retina subsequently receives the sum of this radiation energy for each unit area. Ring-shaped zones around this initial image (corresponding to the enlarging fireball) receive less energy per unit area and radiation of different spectral quality (relatively more "reddish" than the initial radiation).

The initial high radiant emittance and high temperature radiation is of special interest for several reasons. We can assume that an eye will react to the flash with closure of the lids. In man this reflex has a minimum latency of 55 msec. (Brunn, Falk, Matthes and Matthes[24]; Gerathewohl and Strughold[53]), with an average of nearer 100 msec.

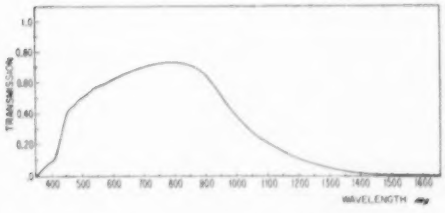


Fig. 3.—Spectral transmission of the human eye, for 400 and 640 mμ, after Ludvigh and McCarthy,[83] and for the wave lengths longer than 660 mμ, after Roggenbau and Wetthauer.[103] The curve has been extrapolated in the ultraviolet, using data from Kinsey.[69] The Roggenbau-Wetthauer data were recomputed from the thicknesses of cow's eyes, from which they were measured, to thicknesses of human eyes.

In rabbits the average lid-closing time was found to be 284 msec. About 35% of the total energy emission of the central part of the fireball (radius, 13,700 mm.) arrives at the eye during the first millisecond (Fig. 2). For this part, the closure of the lids, as well as the pupillary reflex, has too much latency to be of any protective value.

The transmission of the eye is assumed to be similar to the data in Figure 3. This curve is a composite of data from Ludvigh and McCarthy (1938),[83] from 400 to 640 mμ, and the recomputed data of Roggenbau and Wetthauer[103] (1927) for wave lengths longer than 640 mμ. It was extrapolated into the ultraviolet values, taking into consideration Kinsey's (1948)[69] data on rabbits. Data on the absorption of the pigment layer were not available for this study.

For the animal experiments, as well as for consideration of human eyes, refractive error must be considered. The enlargement of the image radius is approximately proportional to the pupillary radius and to the shift of the image from the retina. In human beings we can assume for the large majority that correct focusing would occur by emmetropia, accommodation, or correction of refractive errors. The strain of rabbits used in our experiments had about 2.5 D. of manifest hyperopia. For practical purposes the resulting enlargement of the image radius is negligible (about 0.08 mm. when pupil diameter is 9 mm. and focal length 10 mm.). The increasing size of the actual fireball image, diffraction, and scattering effects would overshadow the effect of small errors in refraction.

The relative opening of the eye differs in different species. A rabbit eye with wide night pupil, about 9 mm., has about twice the relative opening of a human eye with wide pupil, of 8 mm. (the nodal point is closer to the retina in the rabbit). Since irradiance on the retina is proportional to

the square of the relative opening of the eye, a human eye, if absorption were equal, would require at the cornea four times the irradiance necessary for a rabbit at the cornea for the production of a chorioretinal burn.

With equal irradiance on the retina, differences in pigmentation exert a decisive influence on the production of lesions. Radiant energy can produce immediate effects only where it is absorbed. We are dealing here not with a specific effect of certain wave lengths, as in vision, but with nonspecific heat effects from energy absorption. In an unpigmented, albinotic eye, in spite of focusing by the optical system, much radiation will pass through the eye and into the orbital fat. The little that is absorbed in the retina is absorbed in a relatively long path. On the contrary, in a darkly pigmented eye much of the pigmentation is concentrated in the single cell layer of the pigment epithelium, of about 5μ thickness. We can assume that, per unit length of path through the eye and per unit volume, the pigment epithelium in a well-pigmented eye has the highest energy absorption. It is the high energy absorption per unit volume, and not so much the focusing effects, that are responsible for the depth localization of the primary heat effect. This is obvious when we consider what happens in the case of an extended image where no "focal point" is formed.

Since from existing data the threshold for chorioretinal lesions could not be determined, an experiment with sun radiation was performed. A detailed report on this experiment will be given later. Only results pertinent to the present problem will be mentioned here. The experiment was performed with pupils of 5 mm. diameter (rabbits).

The irradiance at the cornea was 0.478 gm-Cal. per second per square centimeter. The smallest lesions obtained had 1 mm. diameter. The assumption was made that 40% of the incident energy was transmitted through the media of these eyes and that all the energy not absorbed was concentrated in the 1 mm. lesion. The energy per unit area for this lesion was found to be 0.14 gm-Cal. per square centimeter. The exposures were about one-thirtieth second. That is far less than the energy per unit area for a minimal skin lesion, and less than reported formerly for eclipse blindness (Eccles and Flynn [45]).

The accompanying Table is an estimate of distances from atomic explosions for 0.1 gm-Cal. per square centimeter in the central image on the retina, which corresponds to the initial fireball of 13,700 mm. No exact data about the spectral transmission of air during different weather conditions are available.

The total air transmission data given in "Effects of Atomic Weapons" (1950) [46] were used. For the human eye a daylight pupil of 4 mm. diameter and a night pupil of 8 mm. diameter were used for computation. The time interval was from explosion to 0.15 second. For the rabbit at night twice the relative opening of the human eye and the time interval from explosion to 0.25 second was taken.

Estimated Relation of Visibility to Distance from Atomic Explosion Which Will Produce Retinal Burns

	Visibility, Miles	Distance, Miles		
		Human Eye		Rabbit Eye, Night
		Day	Night	
Exceptionally clear air	25	36.3	40	49.5
	12	15.7	20	24
	7.2	10.5	13.2	16.5
Clear air	6	7.8	10	12.4
Light haze	1.9	2.9	3.6	4.5

The high initial irradiance of the retinal image has several interesting consequences. If about 33% of the total dosage arrives in 0.001 second, there is scarcely time to dissipate this energy by conduction. The same number of calories arriving during a longer interval of time raises the temperature less because some energy is dissipated during the heating. If, owing to short distance from the fireball, the temperature in the pigment layer reaches more than boiling temperature and there is insufficient time for heat dissipation (as during the first millisecond) an explosion of the boiling pigment epithelium is the necessary consequence. Tissue damage ex-

ceeding the original image in size is then to be expected. Furthermore, it is to be expected that a lesion due to explosion will differ from a lesion in which explosion does not occur, because destruction of individual cells and tissue structure occurs with the explosion.

II. EXPERIMENTAL CHORIORETINAL BURNS IN RABBITS

While computations and threshold determinations indicated that chorioretinal burns could be expected to a distance of more than 45 miles, as predicted by Rose,¶ it was felt necessary to verify these predictions by actual experimentation. For this reason 700 pigmented rabbits were obtained. These were all male rabbits weighing between 4 and 6 lb. (1.8 and 2.7 kg.). It was essential to utilize pigmented rabbits because the pigment in their fundi absorbs radiant energy in the same manner as does a human eye. These rabbits were exposed (one time each) during six different atomic detonations at the Nevada Proving Grounds. These detonations all occurred in the dark under very clear atmospheric conditions.

The rabbits were placed in individual boxes which limited their head motion. They were aligned so that one visual axis was directed at the approximate location of the detonation. Since a rabbit moves his eyes very little, no method of eye fixation was required. They were placed in groups at various distances from the detonation point, starting at 2 miles and going back in one instance to 42 miles. Alarm clocks were set to awaken the rabbits just prior to detonation. In addition, each group was photographed by the light of the bomb itself. This was done by a photoelectric timing device which snapped the picture during the first 21 msec., thus recording it before the rabbits could blink. In this manner the animals with closed or shadowed eyes were eliminated from statistical consideration. The animals were examined ophthalmoscopically within the first few hours after the detonation. Retinal burns were identified, described, and then photographed with a fundus camera. Some animals were killed at once in order to obtain the eyes for study; others were followed for longer periods to determine the subsequent course.

The typical fresh lesion in the rabbit eye as seen with the ophthalmoscope is almost perfectly round, and sharply circumscribed, and consists of a central and a peripheral zone. In animals exposed near the detonation flash (within approximately 8 miles) one sees a deep central hole, with glistening white

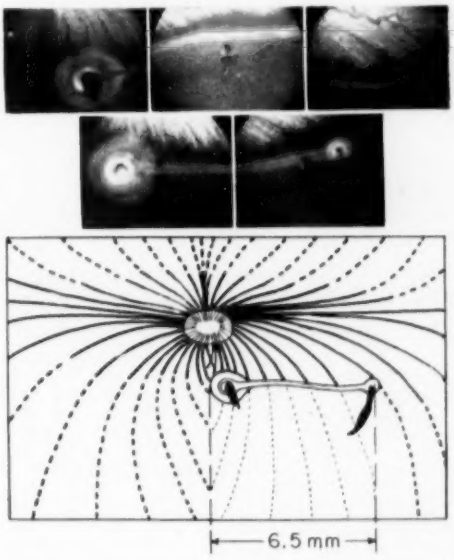


Fig. 4.—Atomic chorioretinal lesion produced in pigmented rabbit eye; unusual case of double disciform lesions connected by linear burn.

Top: Two hours after exposure (high energy).

Center: Two days after exposure.

Bottom: Schematic diagram showing medullated nerve fibers in heavy lines; nonmedullated nerve fibers in dotted lines. The latter have been obtained by extrapolation of the course of the former. Lesion reduced 37% from mag. × 10. (U. S. A. F. Sam R #842).

base, which appears to be sclera. Elevated, volcano-like margins border this area. There may or may not be hemorrhage and/or coagulated debris exuding from the hole. Surrounding the central hole is a "halo" of dirty-gray color, often twice the diameter of the hole. At greater distances from the flash the

¶ Rose, H. W.: Unpublished report, 1953.

Fig. 5.—Top: Early stage of atomic chorioretinal lesion (larger disciform lesion of Figure 4).
Bottom: Microscopic section vertically cut through larger lesion. Coagulation necrosis with major tissue and cell destruction in choroid and retina; exudation and hemorrhage in liquefied center of lesion; bulging and rupture of retina; artificial detachment of retina. Magnification to scale of retinal picture. Hematoxylin and eosin; reduced 25% from mag. × 50 (U. S. A. F. Sam #842-C11).

Fig. 6.—Early stage of atomic chorioretinal lesions. Vertical section through linear burn effect shown in Figure 4. Notice the well-preserved inner layers of the retina. Artificial detachment of the retina on both sides of lesion. Hematoxylin and eosin; reduced 25% from mag. × 150 (U. S. A. F. Sam #842-C1).

central area no longer appears to be a hole but is, rather, a yellowish-white plaque, while the "halo" also diminishes in size with increasing distance until at middle distances it disappears completely, whereas the plaque persists. The remainder of the retina appears entirely normal.

Not all distances were utilized on all shots, and cameras and photoelectric equipment were not available for each station. In addition, the photoelectric device failed to trip the shutters at the 28- and 42-mile stations. Fifteen rabbits were located at each of the stations except the very close ones. The rabbits that were shown photographically to have closed eyes at time of detonation were eliminated from statistical consideration. On at least one of the shots chorioretinal burns were produced in 100% of the animals at each of the following distances: 4, 5, 6, 7, 8, 9, 10, 12, 13, 14, and 27 miles. At the 27-mile station 4 rabbits had closed eyes, and the other 11 had well-defined chorioretinal burns.

At the 28-mile station 8 out of 15 rabbits had retinal burns, but since the camera failed to register, it is not known how many had opened eyes.

At the 42.5-mile station 3 out of 10 rabbits had retinal burns; but, again, the camera failed to operate, so that the real percentage of exposed eyes is not known.

III. PATHOLOGICAL FINDINGS

Material.—Sections of the eyes from a total of 173 pigmented rabbits have been prepared to show the histopathological changes produced within the eye by atomic flash. In this preliminary report a few slides have been selected to correlate with the clinical picture and to illustrate tissue changes accompanying atomic flash burns in retina, choroid, and sclera.

Morphology.—The extent of the microscopic changes in the choroid and retina of pigmented rabbits exposed to atomic flash varied greatly, according to the amount of energy which had been absorbed by the tissues, primarily the retinal pigment epithelium

and the choroidal chromatophores. These histologically visible changes in choroidal and retinal tissues can be divided into two characteristic types:

1. Lesions characterized by coagulation necrosis with additional major tissue and cell destruction in retina and choroid. This major tissue destruction is probably produced by explosive intracellular and extracellular generation of steam and gaseous expansion.

2. Lesions characterized by coagulation necrosis without major tissue and cell destruction in the retina.

Both types can best be demonstrated by an unusual case in which a double retinal lesion occurred, as shown in Figure 4. In this case, two disciform lesions of Type 1, above, were connected with each other by an opaque linear burn, of Type 2. The diameter of the larger discoid lesion was 1.6 mm.; that of the smaller discoid lesion was 0.5 mm. The length of the linear burn measured 6.5 mm.; its width, 0.2 mm. These measurements do not include the secondary choroidal reactive changes seen surrounding the lesions.

Ophthalmoscopically, both discoid lesions showed an immediate rupture of the retina and hemorrhage into the vitreous body. This vitreous hemorrhage disappeared within two days. The tissue around the necrotic center appeared as a gray, milky ring, which measured 1.6 mm. in diameter on subsequent sectioning. After two days the animal was killed for histopathological investigation of the eyes. The pertinent sections are shown in Figures 5 and 6.

The microscopic picture of the larger lesion (Fig. 5) was that of circumscribed coagulation necrosis measuring 1.6 mm. in diameter, with almost complete disintegration of nerve tissue and choroid within a central area of about 0.4 mm. diameter. Hemorrhage from choroidal vessels had produced a circumscribed bulging elevation of retina into the vitreous, with a horseshoe-shaped retinal tear. Although the retinal architecture is seen to be relatively well preserved over this area, the underlying retinal pigment epi-

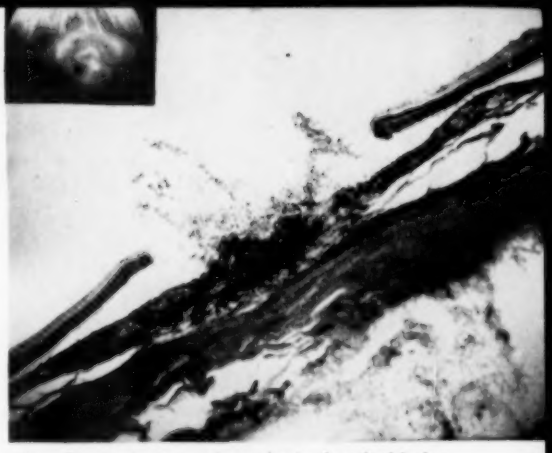


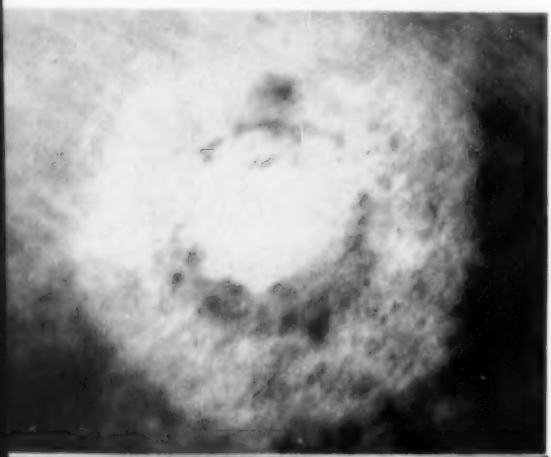
Fig. 7.—Early stage of atomic chorioretinal lesion in pigmented rabbit eye (high energy), killed two days after exposure. Hematoxylin and eosin; reduced 25% from mag. × 60. Insert in left corner shows ophthalmoscopic picture of lesion; reduced 25% from mag. × 10 (U. S. A. F. Sam #309).

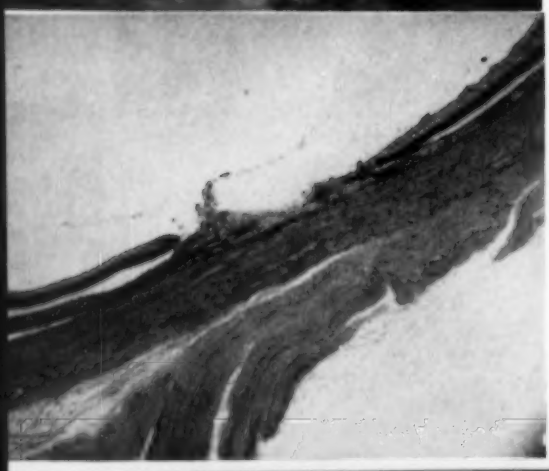
Fig. 8.—Early stage of atomic chorioretinal lesion (high energy). Rabbit killed eight hours after exposure. Notice burn effect in sclera. Hematoxylin and eosin; reduced 56% from mag. × 50 (U. S. A. F. Sam #113).

Fig. 9.—Aseptic inflammatory reaction in early atomic chorioretinal lesion. Accumulation of polymorphonuclear granulocytes, predominantly eosinophiles. Hematoxylin and eosin; reduced 25% from mag. × 200 (U. S. A. F. Sam #844).

Fig. 10.—Late stage of atomic chorioretinal lesion, pigmented rabbit, 18 days after exposure (medium energy). Insert shows ophthalmoscopic picture to scale with microscopic photograph. Note obliteration and cicatrization of choroid in center of the lesion and reactive hyperemia of choroidal vessels in surrounding tissue. Artificial detachment of choroid on both sides of lesion. Hematoxylin and eosin; reduced 25% from mag. × 10 (U. S. A. F. Sam #600).

Fig. 11.—Late stage of atomic chorioretinal lesion, pigmented rabbit, 28 days after exposure (high energy). Advanced scarification of choroid, causing large granulated "halo" in fundus picture. Obliteration of choroidal vessels and pigment atrophy. Hematoxylin and eosin; reduced 25% from mag. × 50 (U. S. A. F. Sam #53).





thelium and choroid have disintegrated. The choroid showed, in addition, dilatation of vessels, moderate edema, and minor hemorrhages.

The histological section cut vertically through the linear portion of the burn of Figure 4 revealed (Fig. 6) marked choroiditis, accompanied by structural changes in the adjacent retinal layer, whereas only minimal alterations occurred in the remainder of the retina.

Retinal and choroidal lesions resulting from exposure to energy levels higher than those which produced the foregoing lesions are shown in Figures 7 and 8, as follows:

Figure 7 is a photomicrograph showing marked destruction of the retina over a central area of 1.1 mm., with choroidal alterations extending to a diameter of about 3 mm. This "perifocal" choroidal lesion seen histologically correlates closely in area with the ophthalmoscopically observed opacity of the retina which had been seen to surround the central area of retinal destruction. It is notable that there is no histologically demonstrable indication of retinal swelling or retinal edema within this perifocal area. One might be inclined to assume that the gray retinal opacity surrounding the central area of retinal disintegration, i. e., the perifocal retinal opacity, represents coagulation necrosis rather than edema.

Figure 8 shows the tissue damage produced by extremely high levels of atomic flash energy. In such severe atomic burns almost complete destruction of the retina and choroid is found, often associated with a widespread coagulation necrosis, which penetrates deeply into the sclera. However, even in severe burns no case of perforation of the sclera was observed.

Figures 9, 10, and 11 illustrate the histological changes associated with healing of these lesions. Figure 9 shows the appearance of aseptic inflammation which developed early in the repair phase. Polymorphonuclear granulocytes are present in the necrotic tissue of all the cases at this stage of repair. In many cases, such as the eye from which

Figure 9 was made, eosinophiles were found to predominate.

The final results of the repair process, after liquefaction, phagocytosis, and digestion of debris had taken place and exudate had been absorbed, was a replacement of the disintegrated nerve tissue by glial tissue. In the choroid many of the dilated vessels were obliterated. Figures 10 and 11 illustrate the conversion of the granulation tissue to dense connective tissue, which provides a relatively firm connection between retina and choroid.

The biochemical changes occurring in these eyes are still being studied and will be reported at a later date.

COMMENT

The animal experiments have shown that danger to the retina from an atomic explosion actually exists beyond previously estimated distances. While the experiments were performed on rabbits, they show, within experimental error, agreement with the estimates made in the Table. It is obvious from studying the burns in question that they do not represent the maximum distance at which they may occur, but that the threshold is being approached. There is, therefore, substantial support for our estimates of threshold distances for human eye lesions as given in the Table. It is apparent that the diameter and severity of the lesion decrease with increasing distance. Near the fireball the predicted explosions within the retina were observed. Near the estimated threshold distances no retinal explosions were observed. One must consider the possibility of an atomic flash burn occurring directly on the optic nerve head. This would, if of sufficient size, result in complete blindness of the affected eye.

From the series of microscopic sections thus far studied, it can be inferred that the pigment of the retinal epithelium and choroid is the principal site of absorption of the energy from atomic flash which produces intraocular lesions. The lesions are characterized by a coagulation necrosis, accompanied by central major tissue destruction involving these same pigmented layers. In lesions caused by low radiation energy, the inner layers of the retina are usually well preserved. This does not necessarily imply functional integrity in vivo, since moderate heat with temperatures below the boiling point may cause coagulation necrosis without destruction of the architecture. Similar cases have been described by Birch-Hirschfeld # (1912) and by Verhoeff and his associates (1916).[123] These investigators produced retinal burns with a carbon arc for the purpose of correlating histopathological changes with the clinical picture of solar retinitis. Birch-Hirschfeld * also observed that thermal damage produced in the choroid and retina of pigmented rabbits is greater than that produced in the eyes of albinotic rabbits. He interpreted his findings as evidence that the anatomic lesions of eclipse blindness are a transudation from the choroid, necrosis of the outer retinal layers, and disintegration of the pigment epithelium, a conclusion already made by Czerny,[14] Deutschmann,[17] and Witmark.[14] According to Birch-Hirschfeld,† the inner retinal layers were only secondarily involved—a conclusion which remains to be proved. There is strong evidence that coagulation necrosis caused by heat below the boiling point of tissue was the cause of the milky-gray discoloration of the retina seen with the ophthalmoscope.

Histologically, this gray retinal tissue was distinguished by a well-preserved architecture. This discoloration could be interpreted not only as the result of a direct heat coagulation of the tissue, but also as the result of delayed autolysis. Such a delay in autolysis could be explained by heat destruction of the enzymes which normally initiate rapid autolysis.

The histological evolution of the tissue repair following these atomic bomb flash burns does not differ essentially from a repair following burns produced by other sources of energy. Remarkable, however, was the extensive accumulation of eosinophiles in some cases. This finding suggests the occurrence

References 13 and 14.
* References 12 through 15.
† References 12, 13, 14, and 16.

of a hypersensitivity reaction to the denatured protein or its derivatives. Also surprising was the extent of the reactive hyperemia in the choroid surrounding the lesion. In some cases it exceeded the area of primary damage by more than six diameters. This observation suggested a study of the heat effect on the activity of certain enzymes in the retina and choroid. This is presently being undertaken. In the final stage of repair, the prominent features of the microscopic picture were the obliteration of initially dilated vessels, the scarification in the area of the burn, and the solid fusion of retina, choroid, and sclera at the margin of the lesion.

These atomic chorioretinal burns are important to the practicing ophthalmologist, who should be aware of the danger of their production for civil defense reasons. Certain facts must be emphasized. A large part of the energy is delivered so rapidly that blinking and pupillary constriction have only limited protective value. Relative pupillary aperture is a most important factor; thus, atomic chorioretinal lesions will occur much more frequently and at larger distances at night. The darker the pigmentation of the retina, the more susceptible it is to being burned. Defects produced in the visual fields will be peripheral unless the burn involves the macula or the nerve head, in which case very severe visual defects may result.

FUTURE THERAPEUTIC POSSIBILITIES

The clinical observation of a sharply circumscribed coagulated area in the fundus, together with the pathological finding of solid fusion of retina, choroid, and sclera, immediately suggested the use of visible and infrared radiations as potential agents in the therapy of such intraocular diseases as retinal detachments, small malignant growths, retinal cysts, and the like. Such small areas within the eye could be coagulated by the focusing of large amounts of radiant energy. Technically the procedure is entirely feasible. Radiation from a carbon arc concentrated by means of lenses will given sufficient energy per unit area. The direction of the beam could be controlled under direct vision by means of partially transmitting mirrors. This method offers the advantage of making unnecessary such surgical procedures as the opening of Tenon's capsule, tenotomy, and perforation of the globe. Therapy in the posterior segment, particularly for central retinal detachments, eradication of small malignant tumors, cysts, and vascular conditions, such as von Hippel-Lindau disease, may be practicable. The first steps toward the development of the technique have been undertaken.

SUMMARY

Potential danger to the retina beyond previously estimated distances is discussed. In exceptionally clear air the nominal atomic bomb (20 KT) can be expected to produce atomic chorioretinal lesions in humans up to 36 miles in the daytime and up to 40 miles at night. Larger nuclear devices would be expected to produce them at greater distances. The results obtained in the experimental exposure of 700 pigmented rabbits to the atomic flash are given. A therapeutic use for visible and infrared radiation of the eye is suggested.

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Paraffin Method of Embedding Ocular Specimens for Microscopic Study

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Paraffin as a medium for embedding ocular tissues is used to a considerable extent in many eye laboratories. While formerly used only for biopsy and autopsy specimens, it is now employed by some for surgical specimens as well. At the Mount Sinai Hospital in New York, we have used paraffin for many years for surgical specimens. Even large, bulky specimens of exenterated tissue are treated by this method. The method has proved to be so satisfactory that in recent years it has replaced celloidin (or Parlodion) embedding as the method of choice in the preparation of all ocular specimens.

Whole sections of surgically removed eye specimens prepared in celloidin have undoubted advantages in that the shape of the globe undergoes the least possible alteration and the relative positions of ocular layers are undisturbed, probably as a result of the slow embedding process. Probably the only additional advantage of celloidin is that the lens retains its consistency to a better degree than in paraffin, in which it may become brittle and break. In paraffin, the cornea occasionally buckles, the globe may be lengthened or shortened, and folds or wrinkles may appear in the cornea and sclera. In both autopsy and surgical specimens in which detailed study of individual layers is desired, the preservation of the shape of the globe is not an important aid in the study; and the minor defects obvious in the outer coats of the eye are not a hindrance. There can be no question that when detail in cells and other tissues is required, paraffin is not only preferable but almost indispensable. For example, the paraffin method is a necessity in the study of general diseases as they affect the retina and choroid, as well as of specific diseases of these layers.

Surgical specimens prepared in celloidin may present numerous disadvantages. In the cornea, intralamellar exudates and cells in the stroma are not easily identified. In paraffin, the stroma bundles are separated to some extent, so that cellular deposits lie free in the spaces thus produced and are accessible for study. Also, the thinness of the preparation allows for easier identification of cells in the anterior chamber, the iris, and the meshwork of the angle of the anterior chamber. In the angle itself, the trabecular bundles are more distinct than in celloidin sections. In the retina, ganglion cells and glia cells and fibers, as well as vascular structures, are more easily studied in paraffin. Particularly in the choroid are the advantages of paraffin striking. This membrane is usually shrunken in celloidin and the vasculature and pigment structure are so fused as to make proper differentiation of the two difficult. In a properly prepared paraffin section, the choroid undergoes minimal shrinkage, permitting better differentiation of its component parts. For these reasons, therefore, the instructional value of normal, as well as pathologic, specimens in paraffin preparations is greater than in celloidin sections.

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From the Laboratories and Ophthalmological Division of the Mount Sinai Hospital.

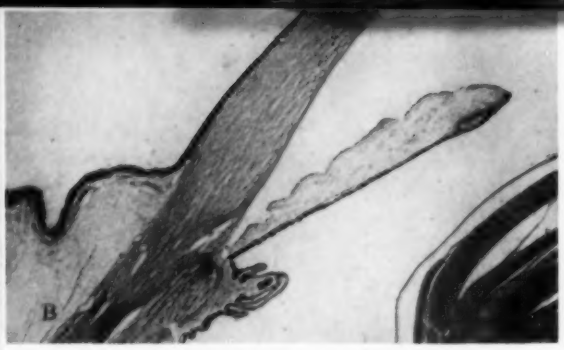

Fig. 1.—Sections of normal globe prepared in paraffin. *A*, section of whole globe; *B*, portion of anterior segment.

Perhaps the most attractive feature to most technicians, and to surgeons interested in the pathological diagnosis of eye specimens, is the fact that an eye processed in paraffin is available for study in 17 days, as compared with the 2-month average period required for celloidin fixation. The shorter

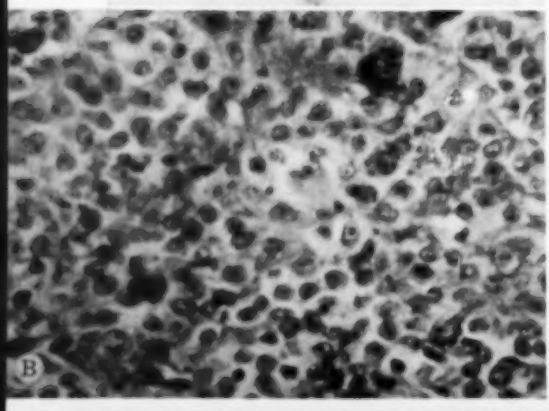

Fig. 2.—Sections of intraocular new growths prepared in paraffin. *A*, malignant melanoma of choroid; *B*, section of malignant melanoma of choroid (cut from embedded hemisphere; reduced ½ from mag. × 458); *C*, retinoblastoma.

technique is particularly desirable in the preparation of specimens of ocular new growths. Also, the thinner paraffin tumor

sections are superior in the ability of the examiner to recognize and differentiate the cellular types in both malignant melanoma and retinoblastoma. Many pathologists, in order to make tumor sections available in three or four days, use the calotte method. When the globe is secured, the sclera is incised and a slice of the tumor attached to sclera or a portion of the tumor tissue alone is embedded in paraffin. The remainder of the globe is then prepared in celloidin. While this method has the advantage of confirming a tumor diagnosis in a relatively few days, the excision of a portion of the globe often results in destruction or damage to tissues adjacent to the tumor. Thus, sections of the remainder of the globe are difficult to evaluate as to tumor extension within and beyond the globe. Such sections are even more unsatisfactory if the globe has been incised before it is properly fixed and dehydrated. Since this, in our experience, requires eight days, it would seem preferable, altogether, to leave the globe undisturbed, since satisfactory whole sections can be prepared in 17 days.

PARAFFIN-EMBEDDING TECHNIQUE

The paraffin-embedding technique for both autopsy and surgical eye specimens as used in this laboratory is as follows:

Paraffin Technique for Eye Embedding.—The steps, in order, follow:

Bouin's solution fixation	2-3 days
Alcohol, 50%	2 days
Alcohol, 70%	2 days
Alcohol, 80%	2 days

The globe is then cut in half anteroposteriorly through the center of the horizonal diameter of the cornea. A straight-edged razor blade is suitable for this purpose. One-half the eye is processed in paraffin; the other half may be run through celloidin, if desired. Further steps are as follows:

Alcohol, 95% (two changes)	6-7 days
Alcohol absolute (two changes)	3-4 days
Xylene-absolute alcohol, equal parts	30 min.
Xylene (two changes)	1 to 1½ hr.
Xylene-paraffin (melting point 48-50 C; equal parts, at 37 C)	30 min.
Paraffin (melting point 48-50 C)	1 hr.
Paraffin (melting point 54-56 C)	1 hr.
Paraffin (melting point 54-56 C), plus Tissuemat (melting point 56-58 C), equal parts	1 hr.
Embed in fresh changes of last paraffin-Tissuemat mixture	
Cool block and keep in refrigerator overnight	
Cut sections at 8μ on rotary (Spencer) microtome with a very sharp knife	

When the preservation of the lens is desired for purposes of later study, clearing in xylene may be prolonged until the lens is cleared. If desired, the lens may be removed and run through separately, more time being allowed for clearing.

Technical Advantages of Paraffin.—1. Thickness: Sections average 8μ, as compared with the average celloidin section of 18μ.

2. Staining: Since sections are floated on and adhere readily to slides after drying, manipulation in staining is easier. Most stains are equally successful in paraffin and celloidin. (The leucofuchsin-periodic acid-Schiff reagent stain cannot be successfully applied to celloidin sections.)

3. Handling of slides: Since two sections are easily floated on a single glass slide, and as many as 10 slides can be stained at once in a dish, continuity of sections is more easily maintained, thus facilitating serial sectioning. Celloidin sections must be stained individually and are not as easily handled.

Factors Essential to Success in Paraffin Technique.—Strict attention to the timing of the xylene treatment prevents brittleness. This is important in the further processing of the embedded material. The sharpness of the knife cannot be emphasized too strongly, since it is the most important factor in securing good sections and reducing to a mini-

Summary of Advantages of Paraffin over Celloidin Embedding

	Paraffin	Celloidin
Total time	17 days	10 wk. average
Thickness of sections, μ	8	16-20
Suitability for histologic study	Details of cell and membranes are clear	Thicker sections obscure details
Shrinkage or compression	Distinctly less, especially in choroid	Greater than paraffin
Appearance of ocular layers	Component parts are more defined	Component parts are not distinct, owing to compression
Handling of material	Sectioned in ribbons, floated onto slides, and stained	Sectioned singly, stained, and then mounted on slides
Serial sectioning	Many sections can be stained at one time	Sections must be stained individually to keep number rotation
Storage of material	Blank slides and blocks can be stored indefinitely	Blocks are frequently lost, owing to evaporation of alcohol

mum the folds that may occur in the cornea and sclera, as well as in maintaining the proper shape of the globe.

It is suggested that the globe be cut in only two hemispheres. The preparation of three or four "caps" increases the tendency for wrinkling of the cornea and sclera and distortion of the contours of the globe.

COMMENT

Undoubtedly, all eye pathologists have recognized the desirability of thinner sections than those available in celloidin. Probably the fear of greater shrinkage in paraffin has deterred many from adopting the paraffin method. Prolonged experience with paraffin embedding has proved not only that this idea is groundless, but, on the contrary, that shrinkage of tissues is decidedly less than in celloidin. The celloidin method, moreover, places a premium on proper fixation of the globe, whereas paraffin does not. If an improperly fixed globe is processed in celloidin, there results, after prolonged hardening in celloidin, deterioration in the tissues, and consequently poor sections. If an improperly fixed globe is processed in paraffin, the consequences are not serious, since the paraffin process is relatively short.

According to information received from 70 laboratories in the United States where eye specimens are processed, two-thirds use celloidin exclusively. The remainder use paraffin, and on the whole are satisfied with the method. However, several are not completely happy with their paraffin sections, since they depend upon celloidin sections for teaching and demonstration purposes. Many use paraffin only for biopsy specimens, and many, as has been indicated, prepare a calotte of the globe in paraffin for tumor and other cases. Some have tried paraffin and abandoned the method.

It would appear, then, that the ideal method for embedding eye specimens is not at hand. Apparently, the paraffin method is gaining adherents, in spite of the rather closer attention required than is necessary with celloidin. With these facts in mind, a method of paraffin embedding is offered in the hope that it may solve some of the difficulties encountered by some who have used this medium, and that others who have hesitated to use paraffin may be encouraged to give the method of fair trial.

SUMMARY

A method of preparing autopsy and surgical eye specimens in paraffin for microscopic study is presented and recommended, for these reasons:

1. It requires one-third the time necessary for celloidin preparation.

2. Sections thus prepared afford greater opportunity for detailed and comprehensive study.

3. The nature of intraocular tumors is better evaluated.

4. The ease of technical manipulation allows for more efficient staining and serial sectioning.

5. Material thus prepared may be preserved and stored indefinitely.

Efficiency and the Ophthalmodiagnostic Process

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Tonight we are met to honor the memory of Charles H. May, and while I must first express my pride and pleasure in being asked to deliver this memorial lecture, this emotion is a little tempered by the responsibility of doing full justice to such a task.

Charles May as a man was preeminently just in his dealings with both patients and colleagues and was sought out by many, particularly of the legal profession, for this reason, as much as for his clear and analytical mind. His courage in the face of crippling accident illustrates the saying that "the fire which melts the wax tempers the steel."

May as a student was brilliant from his earliest days. Since 1879, when he was a pharmacological Gold Medalist, his life was directed by his desire for knowledge. How many ophthalmologists of the last generation could have claimed, as he could, to have crossed the Atlantic 54 times in search of information, and to have been the personal friend of every ophthalmic leader in Europe at a time when European ophthalmology was relatively much more important than it is today?

As a teacher, May utilized the knowledge so gained, as Francis Bacon once said, "to prick in some flowers of other lands into the customs of his own." His textbook, illustrated with his own drawings and rewritten by him time and time again in an effort to achieve semantic and scientific perfection, still influences ophthalmic teachings in England half a century after its first impression. If one looks at the immaculate "Cancelleresca" of his old notebooks, the word which springs to one's mind is "meticulous."

To an English observer, the life of such a man, with its bourdon note of help to others ringing through it, seems to have been based on the aphorism of Hillel, the sage—"If thou are not for thyself who will be for thee, but if thou art for thyself alone wherefore art thou?" The particular aspects of Charles May's life which have inspired the title of my paper are, first, his interest in instrument design—many of today's ophthalmoscopes still incorporate his ideas—and, second, his interest in clinic organization—the Eye Department of the Bellevue Hospital, his foundation, still stands as his memorial. On one occasion the head of a big business corporation, watching his office routine, offered him a post as an administrator.

By the efficiency of the ophthalmodiagnostic process I am referring not merely to the accuracy of tests and clinic routine, but also to the social value they return for a given input of energy. My justification for this attitude is that the cost of medical treatment in England is increasing so enormously that it is beginning to exert a Malthusian pressure against its means of existence. As Ffrangcon Roberts indicated in 1948, this is due (1) to an increase in diagnostic activity out of all proportion to therapeutic gain and (2) to the aging of our population, like yours. One in seven is now, and in 12 years one in five will be, over 60 years of age. An increasing

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The Charles H. May Memorial Lecture.

proportion, therefore, has to be maintained in a state of medicated survival. The "free-for-all-at-the-time" Medical Service, although it is costing two and a half times what was expected in England, has just been instituted in Spain, and may very easily be here before you realize it. The resources to meet the requirements of such a service in England are diminishing. Great Britain, of course, has had a contracting economy since 1909, and, to quote a gloss on Goldsmith's poem:

> "'Ill fares the land to hastening ills a prey
> Where wealth accumulates and men decay';
> But how much more unfortunate are those
> Whose wealth diminishes and population grows."

This is not the case in America, but here you have a large burden of hemispheric defense. In England it is becoming obvious that we shall have to choose whether we shall continue to spend £20 a week educating spastics up to what is euphemistically called "craft level" or forego this, for example, in favor of beds which might return trained and capable tuberculosis sufferers to work. Housing has a particular effect on health with us, as we lost half a million houses in the last war, and we have to consider whether we are justified in commandeering large empty houses as clubs for the mentally deficient, whilst families who are all actively working are crowded into substandard and unhealthy tenements.

We are faced, in fact, with a paradox in medicine, to put it summarily, "The more you can do, the more you must do," a paradox which has raised acutely the question of the nature of the doctor's role in civilization. As has been said rather bitterly by one author, "Every life saved from disease in Asia, becomes a life threatened by famine." This paradox is known in England after the radiologist who formulated it in 1948 as "the Paradox of Ffrangcon Roberts."

Roberts indicates that within the confines of the Christian (and, for that matter, the earlier Hippocratic) ethic which debars euthanasia, the paradox is insoluble. He does, however, suggest in mitigation these measures:

1. That research should be carried out, in the few hospitals where it is feasible, on diseases that reduce working capacity. He regards medical research as peculiarly subject to the law of diminishing return, opposing, as it does, an inevitable termination in death.

2. That the time wasted by the producer in diagnosis and treatment should be reduced.

3. That the doctor's work in the individual case should be eased to increase his output.

4. That we should examine the tests we use to ensure that they are clinically necessary, and are not used from pride in craftsmanship or fear of litigation.

My own feeling is that our effort is not wasted to the same extent as that of the radiologists and the pathologists, but that we are prone to use quantitative tests where qualitative tests would serve. Color campimetry and detailed diplopia recording are examples of the former, while preoperative cultures for cataract operations are a reflection of the latter. The suggestions of Roberts are, in fact, a clear call to apply the methods of the industrial efficiency expert, who is, of course, basically an American conception.

ERGONOMICS OF OPHTHALMOLOGY

Let us first consider the form of ophthalmic diagnostic service that our population requires (and here the visual requirements of your people closely resemble our own) in the fine engineering, textile, and electronic trades. Ninety-six per cent of our population can read the captions of a strip cartoon, and 84%, a magazine article. Our laity, like yours, has an undue faith in the therapeutic value of spectacles. We, therefore, have to do refractions on a very high percentage of our patients. As refractive error rarely causes complete incapacity, a minute wasted by this group is a lost industrial minute. Normally we used to examine male patients first in our clinics, on the assumption that time was more valuable to men, the breadwinners, than to women, the housekeepers. But since the appearance of "Rosie the Riveter," the prototype of woman in industry, this is arguable. Our aging population, with women outliving the men by seven years, leads to a high incidence of degenerative and lacrimal conditions. As Samson Gideon said, in 1749,

"Never sell an annuity to an old woman—they may wither, but they never die."

The English have a problem peculiarly their own—a very high incidence of squint, possibly due to the inbreeding which occurs in a small island. We have another, that we share with all English-speaking nations, which, to paraphrase Rosenberg, might be called *Der Ophthalmomythus des Zwanzigstenjahrhunderts*—"the ophthalmic myth of the 20th century," which probably brings more people to our clinics than any single symptom. This myth runs as follows:

1. Correct glasses preserve, incorrect glasses destroy, the sight.
2. The majority of headaches are of ocular origin.
3. Near work in artificial light is harmful.

Proposition 1 is true, of course, only of amblyopia in children and of an occasional case of congestive glaucoma.

Proposition 2 is iatrogenic.

Proposition 3 is folk medicine.

Some of my colleagues who agree that it is a myth refrain from attacking it, as it brings a certain number of diseased eyes to us that might otherwise come too late, but I would remind you of an aphorism of de Tocqueville which is of universal application *"Il y a une chose pire que de ne pas avoir de principes, c'est de ne pas fier à ceux qu'on a!!"*

MECHANICS OF DIAGNOSIS

The first concern in the efficiency of any process is easy access to the materials employed.

(*a*) *Access to the Patient.*—If possible, the patient should be immobilized throughout the examination. If the discarding of clothes, discussion of the diagnosis, or different tests require movement from the chair in which refraction is performed, this may occupy nearly as much time as the examination itself. Some movement is inevitable, though Thomas, of Nancy, has designed instruments which can be wheeled across two little rails in front of the patient for slit lamp study, ophthalmometry, and other work.

In saving time in directing the patient, directional color has great value. The patient is directed to sit in the *red* chair and to put his belongings on the *blue* table with the mirror beside it. Escorts are directed to the *green* chair. Once the patient is seated, extension of the head is prevented by a headrest, and for rapid direction of the eyes for ophthalmoscopy, the ophthalmoscope light is directed on to a "cat's eye roadstud" placed in appropriate position. These, incidentally, are visible even to people with 10 D. of refractive error. The patient is directed to put the chin on the *white* hollow on the slit lamp or other similar instrument.

As our refraction in hospital is done in a permanently dark room, we use a completely white chair with a straight back bent forward 10 degrees to prevent extension of the head. The upper eighth of the chair back is blackened to prevent interference with ritinoscopy.

(*b*) *Access to Instruments.*—Reduction in energy input does not necessarily require more complicated machinery. I very much doubt whether the refracting unit suspended from a dental type of chair is any quicker or more accurate than the trial frame. It is difficult to reach a conclusion in England, as, of the five colleagues whom I was able to contact who used an instrument of this type, I found that four had discarded it on various grounds, and I wonder whether its widespread use in America is really because of its virtues or is a question of "keeping up with the Joneses." I would suggest that a time study might form a useful thesis. It is agreed that nothing can equal the speed of lens change in this type of instrument; yet it is impossible to accelerate testing mechanically beyond the patient's reaction time. This is well shown by the three-lens test. The lens changes with this test are so rapid in young people that they speed up refraction considerably, but, while the cross cylinder is of value in elderly people, spherical lens comparison is almost useless with it, as they require several seconds in which to decide.

One of the obstacles to the use of trial-case lenses is that the tables to hold them are not well designed, as the various instruments employed have to be taken out of drawers

Fig. 1.—Semicircular working place. Grouping of the refractionometer with trial case, etc. The shelf surfaces are covered with corduroy to stop noise and rolling.

and when put down on the hard surface, clatter or roll. Further, there is rarely room for a vertex refractionometer. The table illustrated (Fig. 1) was designed to be covered with padded corduroy to stop noise and rolling and to give immediate access to every one of the 37 articles I use in eye testing, exclusive of campimetry and biomicroscopy. One light illuminates the two surfaces of the table in the dark, and the minimal size proved ultimately to be 59 by 29 in. (150 by 74 cm.). The useless space in the center of the trial case has been eliminated to make it more compact. The lenses are not covered, as I have found that on those of up to 3 D. fingerprints are more of a problem than dust, and the use of a duster is essential. This table provides what the efficiency engineer calls a "semicircular working place."

OPHTHALMOMETER VS. RETINOSCOPY

The ophthalmometer is in almost universal use on the Continent of Europe—I can say honestly that I do not know a single colleague who uses one in England, where we rely almost entirely on retinoscopy. The instrument is still employed a little in Edinburgh, where they tell me it takes longer than retinoscopy—the figures given me by Dr. T. A. Vos, at a private eye clinic at The Hague, suggest that not only does it take longer than retinoscopy, but it is usually supplemented in this clinic by retinoscopy. It has one advantage to the skilled person—it will indicate the microform of keratoconus (which may waste time in subjective testing), in which vision is often inexplicably poor, and the unskilled person can learn to use it, thus saving the time of a more skilled one. It does not, however, provide the immediate information as to the clarity of the media provided by retinoscopy.

TEST TYPES

As 95% of the test type work in a clinic is refractive, the first practical aim of the test type designer is to outwit the "total" reader, who reads the entire test type at each lens change, in spite of being urged to the contrary. The Maddox single-line type is the simplest way of doing this without moving parts.

One line is required for each eye, and indices are omitted. A rapid change from one to the other can best be obtained by a rotary switch, and from this to the duochrome test and the Maddox spot. The duochrome test seems to be less popular in this country than in England, although we find it one of the most accurate and rapid tests, even with children. The spectra of the colors should not overlap, and should complement each other, and this is not always achieved. Approximately 1 case in 25 requires a numerical or pictorial test, and this can be slid into the frame where necessary.

With the exception of the minute tangent of 1862, there is less agreement about test types than about anything else in ophthalmology. My own preference is for Monnoyer's *"échelle decimale"* with acuities enumerated 0.1 to 1.5, which are written without a decimal point. I am under no illusion, of course, that this designation conveys a fraction. I chose this way, however, as the quickest means of writing. An arithmetical progression must be used to get whole number decimals.

The physiologists, of course, prefer a geometrical progression which is more consistent with Weber's law and relates the degree of sensation to the logarithm of excitation intensity, and produces a distribution of individual variability that fits the classic Gaussian curve. But, after all, I suppose we use a test type hundreds of times as frequently

as the physiologist, I would even go so far as to say that I would agree to accepting single letters as indications of visual acuity if their value could be generally agreed.

I would also like to make a plea for the reflected test type, which makes the clinic architect's and the orthoptist's task much easier. It is possible to abolish its main faults —the visible edge and internal reflection—

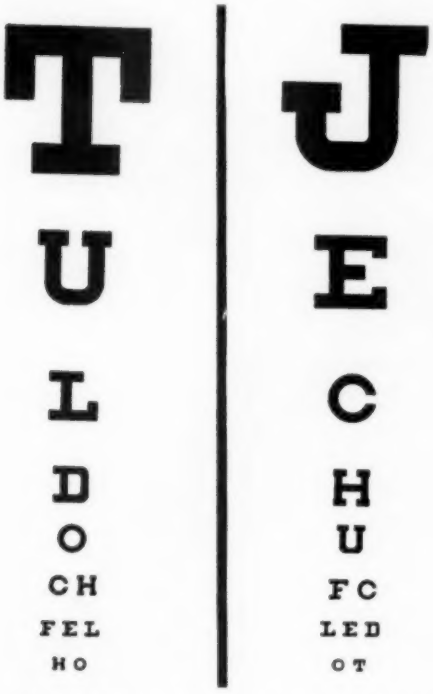


Fig. 2.—Isogonic-isognostic test types. Calculated by Fincham to the designs of Blaskovics.

by using a large, untilted mirror built into the wall.

At present there is no uniformity of "fonts" for the test type in Europe. Those of Landolt, von Ammon, and Birkhauser are in use in various places, and in England there are no less than seven type faces, with differences of 10% in legibility, although the general form of the letters is more or less the same.

In 1916 Zoethout found that a letter "B" of a particular angular displacement required normal vision to be seen at 20 ft. (60 cm.), and an "L" of the same size could be read by an acuity of 0.7. The Landolt ring is no solution of this difficulty, as, apart from the argument that it is a test of light and not of form sense, the C-shape is 15% easier to recognize than those in which the gap is below or on the left-hand side. The ring is, of course, a much slower object to describe than a "declaimable" letter. Blaskovics has produced one solution of this difficulty after 15 years' experiment—the so-called isogonic-isognostic type. These letters not only are of equal angular displacement but are equally easy to recognize. The test type shown (Fig. 2) was calculated by E. F. Fincham for me on this principle. Both 20/20 lines contain a round O, which is specially suitable for cross cylinder testing.

Low-Acuity Test Lamp.—It is sometimes overlooked that accuracy in the range of visual acuity of 20/200 downward is almost as important as the measurement of that above. Snell gives a visual efficiency of 40% to 20/200 and of 3% to 2/200. The measurement of this form of visual acuity is disheartening when one moves the patient toward the test type and his attention is distracted from the top letter by his stumbling feet. I use a lamp which enables the observer to walk in the dark toward the patient, who has only one thing to look at, and the replies of those so tested are astonishingly sharp. It is very simple to make test figures for children by painting on opal Perspex plate with soluble black cellulose.

Reading Tests.—Timing shows that the older the patient, the longer it takes to determine his reading correction in proportion to that of distance, and the more difficult it is to determine whether a change in existing spectacles will improve his reading capacity. De Lapersonne invented a reverse reading type in which the first word was bigger than the last, and as reading tests are done only at intervals of some years, there is no need for a long paragraph. I have adapted this to the device shown (Fig. 3)—the distance of the punctum proximum is easily determined, and the effects of a small addition

Fig. 3.—Reading test. The patient cannot read more than a dozen words at most, and an improvement in reading vision is immediately apparent. Rotation brings the heterophoria test into action.

make an increase in visual acuity immediately apparent, as one cannot deduce the next word from its predecessors. The type is Times Roman, recently adopted as standard by the British Faculty of Ophthalmology, and runs from 24 to 5 point.

The near-point rule shown (Fig. 4), using Duane's figures for accommodation and P. C. Livingstone's for convergence, is so made that it can be brought into position with the movement of one hand. It is only 50 cm. long, and it is rarely necessary to use anything larger than this. The design in general follows that of Berens (1947).

Objective Acuity Testing.—The development of various devices for quantitative stimulation of railroad nystagmus by Goldmann, of Berne, and Ohm offers a way of shortening enormously the time taken to test malingerers and amblyopes. Unfortunately,

these devices, based upon the development of railroad nystagmus quantitatively, have not yet come on to the market.

HETEROPHORIA TESTING

In spite of the application of 50 years' mathematical ingenuity to the figures obtained from heterophoria tests, it is still impossible to assign absolute values to them.

Scobee even showed statistically in 1948 that, contrary to general belief, it is impossible to relate them directly either to the patient's age or to his power of voluntary convergence.

Prismatic prescriptions are also rarer than is believed. Trevor-Roper found only 60 among 25,000 at Moorfields in 1952, nor were these invariably helpful.

The first requirement of a heterophoria test is, therefore, that it should immediately separate the small number of cases of significant heterophoria from the others, and the second that it be capable of quantitative extension.

At 6 meters a Berens Maddox rod, incorporating a 0.75 prism in a cross cylinder handle, does this admirably. Fifteen words of explanation and four in reply are all that are necessary. This test takes 16 seconds, as compared with 66 seconds for the Maddox rod and loose prisms. Thorington's test, invented in 1932, can be used in conjunction with this at 33 cm., taking 25 seconds, as compared with 71 seconds for the Maddox Wing, whose readings (according to Scobee) are almost identical. I have attached the reading test to the back of this to permit the assessment of a vertical prism immediately by simple reversal of the test without further lens change.

DIPLOPIA TESTS

Most analyses of diplopia are far too elaborate. The information required for clinical work is limited to (1) exclusion of low-grade diplopia as a cause of vertigo; (2) an estimate whether cyclophoria is too marked, or deviation too variable, to allow the use of prisms; (3) determination of which muscle one must operate on and when, and (4) the extent and locality of the residual area of diplopia, to give some idea of its effect on function. For this purpose I have modified the Lancaster test slightly, as this gives the answer to question 1 in a few seconds and supplies the rest of the information required in five minutes. I shall not describe the Lancaster test, which is well known here in the country of its inventor—all I have done is to modify the background and method of recording, to superpose both on the same chart, together with the area of binocular vision. To save space, the Lancaster test can be mounted on the reverse side of a Bjerrum screen. The most convenient material for this a ¼ in. (1.8 cm.) balsa board, which, being light and soft, holds pins well and is easy to lift. Arrangement of the test objects for both tests and their rapid use is made on a special stand.

Fig. 4.—Accommodation rule. This rule is brought into action by a single movement. The back of the reading test carries a Thorington test for heterophoria at 33 cm.

GLAUCOMA TESTS

Although the initial diagnosis of glaucoma may be made visually, in many cases its exclusion or confirmation requires the use of campimetry—a form of testing which is also required in following up many of these cases.

No test reflects so strongly the personality and power of observation of both patient and examiner, and an enormous waste of time occurs in attempting to apply it to the elderly and the unobservant, and often to patients with uncupped optic discs. This time is increased if the instruments employed are not self-recording—the prejudice against the use of which I have never been able to understand.

The anomalous results so obtained are liable to produce in the young ophthalmolo-

gist that state of mind described in the phrase of Tacitus "Acribus initiis incurioso fine"—"Early zeal leads to neglect."

The Anglo-Saxon countries have a curious faith in the digital estimation of tension, which is not shared by others. I am well aware that unless tonometer-checking stations exist inaccuracies in these instruments may occur. If we accept them, however, as doing no more than indicating high, middle, and low pressures, the failure of digital observation, even when the method is applied by experienced ophthalmologists, is about 33%—this has been clearly shown by Müller, of Basel, who, with four colleagues, examined 316 eyes in this way.

I never ask a patient whether he has seen a halo, as a certain number are color-blind and others are incapable of absorbing the description. The use of a thin layer of Lycopodium powder between two plates of glass in a trial lens saves minutes of description and gets a clear "yes" or "no" as a response.

TIME EFFECT OF NEW DEVICES

Timing of the application of new devices in my own practice, without a conscious attempt to hurry, showed (first series of cases) a material reduction in the time spent on axial refraction, increasing with use (second series) to 40%. This was partly offset by an unconscious increase in the time spent in obtaining the history and in "exegetics." Conventional methods were used in the following time study of hospital refractions, and it remains for experiment to show whether in so personal a technique as refraction similar reduction can be obtained by others with the instruments described.

It is certain that increase of the number of tests in a given time would enable a better grasp to be obtained of a case and would reduce that tendency, so apparent in a busy clinic, to make certain tests the subject of a further visit or visits and to make, as the song says, "mañana, the busiest day of the week."

IRRITATION POINTS

Ophthalmodiagnostic technique is a peculiarly personal matter, especially the refractive portion of it. Some of my suggestions may be quite inapplicable in America. There is, however, one concept of the efficiency expert which is of general application, "the irritation point."

As the Romans said, "Vexatio dabit intellectum" ("Knowledge comes from annoyance"), and anyone might gain information from applying the points to one's practice.

The obvious ones include "Damnation"—the beginner's reaction to tedium, suppressed by training; "dissonance," due to reverberations from hard walls, floors, and corridors, and "diaphoresis," from stuffy atmospheres.

Less obvious is the "discarding" of tests to which lip service is paid, but which in many offices are covered with dust; and the "delegation" of tests to unskilled personnel without the provision of instruments which permit of a "transfer of skill." Examples of this can be found in scotoma plotting and the verification of spectacles.

Finally, "delay"—this has become accepted in many hospitals as inevitable, but it is in this field that the greatest possibilities exist.

LOGISTICS AND PROCESS FLOW

Timing of a variety of medical, surgical, and ophthalmic clinics by the Nuffield Trust showed that, although my own was the best in this respect, the patients waited 54.8 minutes on an average for 8.2 minutes of medical attention, a figure which obviously offers room for improvement.

In one year 39,000 consultations (this includes 2800 casualties but no orthoptic visits) are dealt with by seven qualified persons (six doctors and one optometrist). Here, if Prof. Ida Mann's figures for 1946 are correct, we see a most striking contrast with the U. S. A. For similar numbers in the United States, a medical staff of 29 was employed. If this is the regular ratio here, while my approach is still valid, my figures are little guide.

The peak attendances were at the 9:15 a. m. "casualty" and the 2:00 p. m. outpatient clinics, so that the plant was used fully for only part of the day.

The average wait between arrival and first examination was 29 minutes, and between the consultation and their test or treatment, 20 minutes. This suggests (*a*) that there should be better coordination between the rate at which appointments are made, and (*b*) that the capacity of separate sections of the department should be adjusted to agree with the rate of the patients' arrival there.

Three arguments are usually advanced against doing this:

1. "Patients don't keep their appointments." We timed 253 patients; 29 were punctual; 167 were early by an average of 21 minutes, and 58 were late by an average of 11 minutes. In other words, in point of time these figures cancel out.

2. "Consultation times vary greatly," the extremes being 28 seconds and 20 minutes, and the average, 4.41 minutes. If patients had been given appointments at this interval, the maximum wait would have been 29 minutes instead of 113 minutes.

3. "Consultation times vary unpredictably." Brigadier Welch, of the Nuffield Trust, and Dr. Bailey, of the Cambridge Department of Human Ecology, showed in 1952 that for queues of patients whose individual processing takes an unpredictable time a certain statistical regularity emerges in the form of a Pearson type III curve. Once the average time of processing and the interval that the doctor can afford to be idle have been decided, the optimum interval between appointments can be determined from this.

TIME STUDY OF THE OPTICIAN

I am open to correction, but so far, I believe, you have no hospital optometrists. Though the idea may startle you, I can assure you we are most appreciative of their work.

On an average, an optometrist completed one refraction in 10 minutes. This is not long, but many of these examinations were repeat checks of existing glasses and other patients were so nearly blind that refraction was discontinued after the first minute or so.

As it was found that one attendance (not one patient) in five involved a refraction, if it was arranged for a surgeon to see one patient in four minutes, then an optician can do the refractive work for two surgeons—a rather surprising finding. The calculation is $\frac{5 \times 4}{10} = 2$.

TIMING OF SECRETARIES

The secretaries had a rather ill-defined task, which varied with the surgeon. Standing by and taking notes (about 31% of their work) is particularly uneconomical, as in 140 minutes' standing by a surgeon, the secretaries spent only 9 minutes in actual stenography. This suggests that a dictaphone is a much more economical proposition. Another 39% of their work could be eliminated by the redesigning of the department.

It was finally suggested that as their duties they should select the notes (20 seconds); deprive patients of their hats, bags, and escorts—608 patients brought 305 escorts—(15 seconds); measure the spectacles—of one patient in five—(45 seconds); do a visual acuity test for distance with glasses (60 seconds); redirect the patient and for general conversation (60 seconds). To facilitate this, colored direction lamps (permanently switched on) are provided over the doors in the final plan.

On leaving, the patient should be given a new appointment by the secretary, and conversation about this is estimated to take 50 seconds. That is to say, the secretary should deal with one patient at about the same rate as the surgeons—four minutes.

At this point it becomes clear that the basic team in a clinic should be a secretary (taking four minutes a patient), a registrar (four minutes a patient), and an optician (10 minutes a patient). As registrars are permitted by the Faculty of Leeds Infirmary only to do "follow-up" clinics, except in the official absence of the chief, it would be necessary to select the patients especially of this type when the registrar was unaccompanied by the chief. To meet 700 attendances a week at the rate of 45 per three-hour ses-

sion would require 16 surgeons' sessions; that is to say, the (*a*) registrar team in a morning, five days a week for three hours, and the (*b*) registrar team five afternoons a week, plus a chief on four of them. A houseman would be required for two morning sessions of three hours and would be mainly occupied in dealing with casualties.

A team must be regarded not as a baseball team, but as a football team, all of whose members must be on the field simultaneously, otherwise congestion will occur.

The dispensing optician was not dealt with in this study, as there was little delay for patients seeing him.

ORTHOPTICS

The time study of orthoptists shows that of the 20 minutes spent on each treatment little time is wasted, but that of 12½ minutes taken for each inspection a certain amount of waste occurred in visual acuity testing of nonoccluded eyes. This was due to distraction of the child's attention by other children and the to-and-fro walk of the orthoptist while pointing to the illiterate test types. The value of cubicles and the reflected type for this work is well shown by comparing the figures for Manchester (average 1.38 minutes per test), which uses them, with those for Leeds (2.21 minutes), which does not.

NURSING

The syringing of tear ducts, tonometry, certain dressings, and treatment of corneal ulcers are carried out by nurses. One attendance in three was found to require this service, the average time taken being 4.36 minutes. At the rate of 15 consultations an hour, half the time of a nurse should be available for other duties, and it is suggested that if the Dangerous Drugs Act allowed it, she might actually dole out the medicines to patients.

DISPENSING

Prescription Delay.—As ophthalmic patients attend frequently for observation, they do not require many changes in their prescriptions, and pass through the clinic much more rapidly than do patients of other types, the requirements of a separate prescription for each patient with the legal hospital minimum of details (identity of patient and prescriber, amount and nature of drug, and the date, traceable for two years) requires a lot of writing.

Analysis showed that 84% of all prescriptions could be covered by the 10 printed cards I introduced in February, 1948, whose only novelty lies in the mnemonic color code (for example, green for glaucoma, red for hot bathing), printing of, for example, four different types of drops for treating conjunctivitis on one card, three of which are crossed out, and the "tear-off" treatment section which the dispensary gives the patient with his drops, saving many explanations. A special box allows the card to be selected by the left hand and signed with the other, with a minimum of movement.

I had hoped further that as writing (legally) includes printing for the name of a drug, a combined signature and date stamp might be employed to replace writing. The legality of this particular point is undetermined, however, and the pharmacist could, therefore, object to a prescriber thus identifying himself.

Dispensing (Drug Issue).—It was found that the queue at the central dispensary, 70 yd. away, led to great delay. Dispensing averaged 10.25 minutes per patient, of which 30 seconds only was occupied in issuing drugs. It would be much better, therefore, if the patients could obtain their drugs in the Eye Department. Unfortunately, the shortage of pharmacists means that one could not be spared for the department itself, and the senior pharmacist objected to the medical staff issuing them on the grounds (*a*) that it would mean labeling bottles, which has never been done (though why is not clear), and (*b*) that the Pharmacy and Poisons Act, 1933, paragraph 26, states: "In any institution in which medicines are dispensed in a Pharmaceutical Department in charge of a person appointed for the purpose, all poisons other than those issued for use within the

institution should be stored in that department." It is interesting that the word "stored" is employed, and not "dispensed," and I cannot help wondering whether the legal requirements would be satisfied by bringing the more commonly used medicaments to the department in a wagon and wheeling it back when the clinic was over.

We have not proceeded with this, however, as now that a patient has to pay 1s. for each prescription, its collection is an added complication.

TEACHING

Only a small percentage of patients provide physical signs for elementary teaching of students, and only a proportion of these are temperamentally suitable. It is possible during student teaching to make the explanations of information or of comfort to the patient, but whatever one does, the patient is bound to be delayed. This situation becomes progressively more complicated, and in one big center three patients in the past two years have threatened to sue the hospital for the delay occasioned by their being used for teaching purposes. The whole problem is so difficult that in a recent discussion on medical teaching a "panel of whole-time patients" was suggested. The solution adopted here is based on that used at Edinburgh, where the subject of clinical ophthalmology is divided into 30 lectures and clinical and didactic teachings are combined. The lecture delivered in the theater next the department is determined by the cases in the clinic. At the end of the lecture (carried out with lantern slides) these illustrative patients are produced for demonstration. This arrangement has the advantage that the minimum number of patients are delayed and that the physical signs which are difficult for the student to see are clearly indicated in the pictures. Tuition in the use of instruments is also essential in our branch of medicine and is obtained at Edinburgh by 10 separate demonstrations of ophthalmoscopy and retinoscopy, which the students carry out on each other, again without delay to patients.

Since writing this, I have been made aware of the possibilities of the transparency viewer, which allows one to demonstrate the points to be observed to a small audience. Theodore Hamblin has developed an attachment to the ordinary 35 mm. film projector for this purpose.

I have found a transparency viewer, or the Hamblin attachment for a small projector, ideal for this purpose. It was found necessary to photograph or commission paintings of slides of ordinary conditions. Existing ranges consisted largely of curiosities or were lacking in the principle of contrast shown here. It was also necessary to create "colloquial classifications" suited to this style of teaching.

DESIGN OF BUILDINGS

Just as the appointment system can be made flexible to allow for absences by the surgeon at committee meetings, some emergency, or even holidays, so it is suggested that a basic cubicle design should be employed which would give the patient the privacy all hospitals lack and which could be converted for the use of any member of the "team." The cubicle is designed so that the switches are standard at two points, as is the mirror type. The door is curtained for privacy and is large enough to take a wheel chair. A "hatch" is also arranged so that the secretary can pass notes through to the surgeon, while there is also room for a few students to be taught and one seat for an escort if it is essential that he enter with the patient.

The size is also determined in part by the use of the so-called modular system. The module, 3 ft. 4 in., is an idea of the architect Le Corbusier, who described his designs for houses as *machines à habiter*. The unit is based on average shoulder width and floor-navel distance, as standards. The whole department is altered by the insertion of these cubicles, and a new color scheme has been suggested. White is painted around the windows and facing them, as well as for the ceiling, as this has been found to be the most pleasant color for this purpose, and pink or

green (with the same, or lower, reflection coefficient) for the walls at right angles. A particolored scheme is chosen here for the sake of making the room more interesting. In order to get rid of noise, the floor is to be of cork and the ceiling of diacoustic units (perforated fiber board) backed by glass wool. The question of coolness without noise can be dealt with by Ventaxia fans, which are silent.

One view of the efficiency engineer is epitomized by the story of the machinist who, after being given tasks for each hand and foot and, finally, his head, was asked for suggestions and said that the attachment of a broom to the back of his belt would enable him to sweep the surrounding floor.

As you will have seen from my account, the efficiency engineer aims to improve the lot of all concerned in a given department. Whether this technique, so successful in the industrial field, will succeed in meeting the emergencies of hospital life, committees, illnesses, holidays, restrictions of registrars to follow-up clinics (except during officially sanctioned absence of the chief), and so forth, is something that only trial will reveal. It is also interesting to note that this "spread-out" of appointments may permit of reduction of one nurse, one secretary, and some orthoptics staff.

Unfortunately, this scheme remains a tour-de-force, as, owing to building difficulties in England, I have been unable to carry it into full effect, though similar designs are working successfully in other British clinics.

EXEGETICS

Guérir quelquefois, soulager souvent, consoler toujours. —Trudeau

When I sent this paper to Dr. Ffrangcon Roberts, his reaction was most interesting. "This assembly line belt system," he wrote, "is rather horrifying; but I suppose it is the only possible answer to universal invalidism."

His first thought was, in fact, of the psychological side of the problem, which is so prominent in ophthalmic patients. The "ophthalmic myth" is a wonderful net for neurotics, whom nothing will cure but a change in milieu, and in so many degenerative cases there is no cure but "earth on the chest." Reconciliation of the patient to his symptoms may be the hardest and slowest part of our task. The first essential is an explanation of the location and nature of the disease in terms which the patient's mind can both grasp and tolerate. An unblown glass eye, for instance, has saved me hours in explaining "myopia" and "astigmatism," believed by many to be diseases rather than deformities.

Sometimes a link with ancestral eye disease comforts the patient so much that one wonders whether he had regarded his trouble as due to divine retribution.

Lewis Carroll, in his poem "The Hunting of the Snark," hit on a psychological truth when he said, "What I tell you three times is true." Even the use of this device in explaining the disease process to a patient may leave his face blank with incomprehension until, at a chance phrase, his face lights up.

I have come to call these phrases key words—"key words" because the differences in educational background of doctor and patient are greater than we realize. An English laborer who tells you his "nerves are shattered" may literally visualize a nerve tonic advertisement, with gaps in the lines here and there.

Such phrases—"rheumatism," "anemia," "blood pressure"—are comforting, because vague terms rarely indicate serious trouble. They give with organic disease a continuity of mental perspective, while they provide the neurotic with a socially acceptable label on which he can "dine out." Such phrases vary with nationality and suffer a declension with social position, for example:

"It's your age Mrs. Bloggs"; "You aren't getting any younger, you know, Mrs. Smythe"; "Anno Domini, I'm afraid Mrs. Bassington-Bassington," terminating in the magnificent verbal guillotine attributed to Sir William Gull—"Nature never forgives and never forgets, dear duchess; that will be three guineas precisely."

I am sure that a study of such specific phrases known to the psychologists under the generic term of "communication" would enable us to comfort far more people and far more quickly than we do today. Care must be taken in their application, however, that in pandering to the undue nominalism of the lay mind we do not lose sight of the true facts as we see them, and that such semantic stereotypes have an agreed meaning. As Lord Melbourne once said to his cabinet, "I do not mind what damned lie we tell, gentlemen, but no man leaves this room until we have decided which damned lie it is going to be!"

In conclusion, my thesis is in part in tune with the American feeling for efficiency as an ideal, but in part runs counter to it in suggesting that indefinite expansion of facilities is not the solution to all problems. I would remind you, however, of the words of Appollonius, in the "Satyricon" of Petronius, which, in principle, underlie all intellectual endeavor.

"Artis severae si quis ambit effectus,
Mentemque magnis applicat prius mores
Frugalitatis lege poliat exacta."

"If any seeks for success in stern art and applies his mind to great tasks, let him first perfect his character by the rigid law of frugality."

Quinine Amblyopia

Report of a Case

MILTON H. LINCOFF, M.D., St. Louis

The case of quinine amblyopia to be reported is considered of interest for several reasons. First, since the amblyopia occurred during a period of hospitalization for another condition, the opportunity arose for immediate, as well as continued, close ocular observation. Second, corticotropin (adrenocorticotropic hormone) was employed in the treatment of the quinine amblyopia.

REPORT OF CASE

A 48-year-old white man was admitted to the surgical service of the Veterans Administration Hospital, Jefferson Barracks, Mo., on Oct. 5, 1953, for treatment of a peripheral vascular disorder of the lower extremities, manifested by intermittent claudication and deficient pedal pulses.

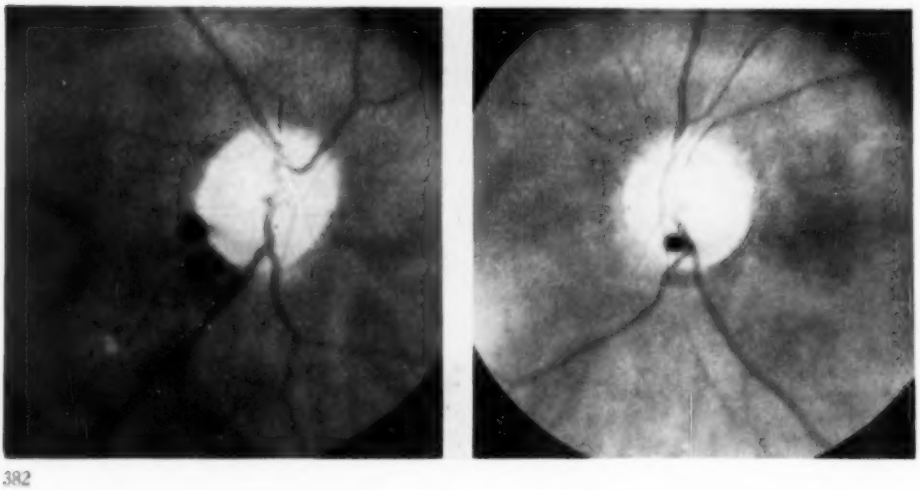
The patient was first seen by members of the ophthalmology department four days later, within 45 minutes after he developed sudden complete bilateral blindness, associated with dizziness, flushing, vomiting, tinnitus, and partial bilateral deafness. Review of the medication revealed that the patient had received a total of 0.8 gm. of oral quinine sulfate in 0.2 gm. doses during the preceding two days, the last dose being given two hours before the onset of blindness. He had also received a total of 1.4 gm. of oral quinidine sulfate in 0.2 gm. doses starting four days before, but this medication had been discontinued 28 hours before the onset. The dose of both these drugs was well within that recommended.

Immediate eye examination revealed the absence of light perception bilaterally and widely dilated, fixed pupils. The extraocular movements were normal. The optic discs were well marginated and pale, particularly in the left eye. The arterioles were markedly constricted, beginning at their emergence from the disc. In some areas they were constricted to mere threads. The veins appeared normal, and the maculae were slightly granular with shimmering reflexes. Only a few localized areas of edema and exudate were present (Fig. 1).

It was felt that this dramatic reaction to such small doses of quinine represented a type of hypersensitivity reaction, since many people take much

From the Veterans Administration Hospital.

Fig. 1.—Quinine amblyopia



larger doses over long periods of time without apparent ill effect. This prompted the immediate trial of intravenous corticotropin in an attempt to block this severe reaction in some manner. However, it did not seem justified to withhold other treatment in order to evaluate the adrenocorticotropic hormone.

ment was continued for two weeks, and then the intravenous administration of corticotropin was gradually decreased and stopped. Oral nicotinic acid with vitamin B_{12} and thiamine was then substituted for the intravenous therapy.

Eight hours after treatment was instituted, the vision was light perception, and hearing was im-

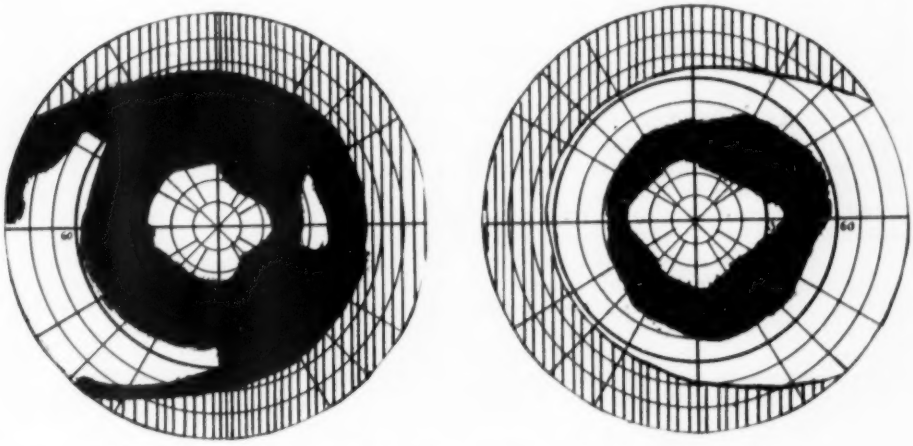


Fig. 2.—Visual fields for 20/330 white three and one-half months after onset.

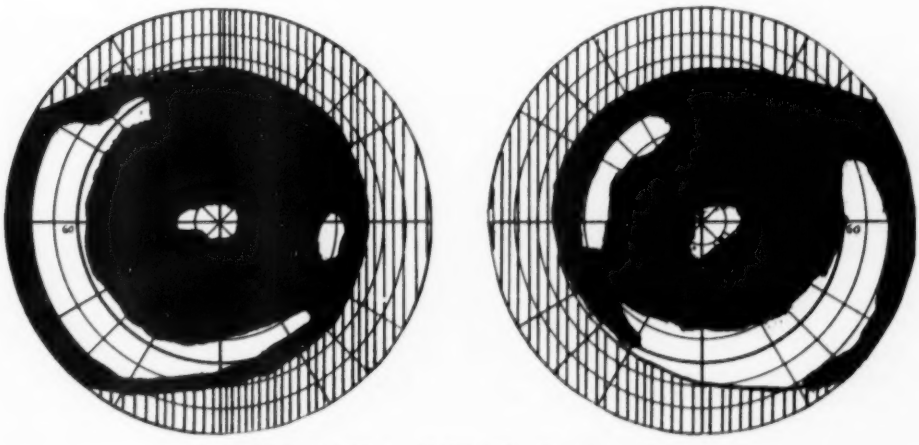


Fig. 3.—Visual fields for 20/330 white 11 months after onset.

Immediately the quinine was discontinued, and a regimen of treatment was instituted with a daily liter of 5% dextrose in water containing 20 mg. of corticotropin with 1000γ of vitamin B_{12} and 300 mg. of thiamine administered intravenously over a 10-hour period. An intravenous vasodilator was also given in the form of tolazoline (Priscoline) hydrochloride, 25 mg. three times a day. This treat-

proved. On the following day the vision was correctible to 20/20 O. D., and 20/25 O. S., and the pupils reacted slightly to light. However, the fields at that time were constricted to a few degrees of central fields with steep edges. The vision improved to 20/20 O.U. after the first few days, and the field rapidly improved and stabilized over a three-month period to that shown in Figure 2. With a smaller,

3/330 white target the left visual field was 5 degrees smaller centrally and the ring scotoma extended to the periphery in the superior temporal portion. The right visual field was just slightly smaller with this target.

Frequent observation during the course of treatment revealed that the optic discs initially became slightly less pale, but then, after one week, gradually became waxy. Over a three-week period the few exudates gradually were replaced with small atrophic areas. The arterioles remained of the same caliber for the first 10 days, and then the often-noted paradox, that is, further arteriolar constriction in spite of the gradually improving field, was observed. Repeated fundus examination during and after intravenous vasodilator therapy revealed no observable dilatation of the vessels.

Another interesting fundus phenomenon was noted in this case. The arterioles were constricted maximally at the disc, and some remained of the same caliber or even dilated slightly, rather than narrowing in the usual manner, as they coursed peripherally.

At the follow-up examination, three and one-half months after the onset, the vision remained 20/15 and the field appeared stabilized. The patient apparently had little difficulty in adjusting to his decreased field of vision.

Occasional tinnitus remained, and an audiogram was indicative of slight nerve deafness consistent with that found in quinine intoxication. For practical purposes the hearing was normal.

The patient did not return for examination until seven months later, stating that the vision had gradually become poorer. Vision was correctible at this time to 20/20, but the visual field had markedly decreased, as shown in Figure 3. The visual field with a 3/330 white target was only very slightly more constricted. The patient showed pronounced difficulty with ordinary ambulation, especially in reduced light. The fundi were unchanged except for the addition of slight diffuse pigmentary change.

Though the prognosis for improvement of vision was considered practically nil at this time, a course of daily intermuscular injections of 500γ of vitamin B_{12} was administered for 12 days and the injections then continued twice a week for 4 weeks. The patient was also given 50 mg. of nicotinic acid three times a day. There was no subjective improvement or improvement in the visual fields.

Mycotic Infection of the Eye

Monosporium Apiospermum Associated with Corneal Ulcer

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Although dermatophytes occasionally infect superficial portions of the mucous membrane and skin of the eyelids, primary and secondary mycotic infections of the eye are relatively rare. Birge [1] recently published an excellent comprehensive review, with more than 300 references, dealing with infections of the eye caused by fungi and fungus-like higher bacteria. Therefore, a detailed summary of the literature would hardly serve any significant purpose in this paper. An extensive review of many published papers on the general subject failed to disclose any instance in which Monosporium apiospermum was associated with corneal ulcer or other infection of the eye. The purpose of this paper is to present the clinical and pathologic observations in a patient with corneal ulcer and hypopyon which failed to respond to antibiotics, sulfonamide drugs, or other therapeutic measures, which are usually successful. M. apiospermum was cultured from the lesion, and fungi were demonstrated in histologic sections of the eye. Inasmuch as Micrococcus pyogenes var. aureus (Staphylococcus aureus) was present also, one cannot be certain as to whether the fungus was the primary causal agent or a secondary invader. However, failure of the lesion to respond to antibacterial agents, in doses usually adequate, indicates that M. apiospermum played a significant role in the disease.

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CLINICAL HISTORY

A white married farmer, 39 years old, had experienced excessive tearing of the left eye for 17 days, with pain in the left eye and jaw for 14 days, prior to admission to the North Carolina Baptist Hospital. A few days after the symptoms began, the patient consulted a physician, who noted an ulcer of the cornea and started treatment with atropine and cortisone. Shortly thereafter the patient consulted another physician, who began treatment of the corneal ulcer with an intramuscular injection of penicillin. The intensity of the pain seemed to increase, and no objective signs of improvement were noted after a second dose of penicillin. At that time the patient was sent to consult one of us (R. W. R.) for further treatment.

Significant physical findings were limited to the left eye. The bulbar and palpebral conjunctivae were fiery red, and a relatively large ulcer involved all the cornea except for a small band superiorly. A collection of opaque, gray-white exudate was present in the inferior portion of the anterior chamber. The fundus was not visualized satisfactorily, although the red reflex was observed through the superior band. The previous diagnosis of corneal ulcer with hypopyon was confirmed. Examination of the right eye revealed no significant abnormalities. The patient's teeth were carious and in generally poor condition, and a Grade I "blowing" murmur was heard over the apex of the heart. Otherwise, all observations made in a complete physical examination were regarded as being within normal range.

Laboratory examinations performed at the time of admission revealed no unusual findings except for leucocytosis. The total number of white blood cells was 16,600 per cubic millimeter of capillary blood, with a differential count as follows: segmented neutrophiles, 69%; nonsegmented neutrophiles, 5%; lymphocytes, 21%; monocytes, 2%; eosinophiles, 2%; basophiles, 1%. There were 5,500,000 erythrocytes per cubic millimeter, and the hemoglobin content of the blood was 16 gm. per 100 ml. A specimen of urine revealed a specific gravity of 1.005. Tests for albumin and reducing sugars were negative, and no abnormalities were noted in the microscopic examination of centrifugated urine. The Eagle complement fixation and standard Kahn precipitin tests revealed no serologic evidence of syphilis.

During hospitalization the rather severe pain in the left eye was alleviated by meperidine

(Demerol), codeine, acetylsalicylic acid, and phenobarbital. Material scraped from the corneal lesion was cultured, and treatment was started with ordinarily adequate doses of fortified penicillin, meth-dia-mer-sulfonamide (triple sulfonamide) emulsion, sulfacetamide, dihydrostreptomycin, chloramphenicol, and atropine. In addition, warm saline compresses were applied to the eye, and, approximately on the third day, there seemed to be slight improvement in the general condition of the eye. However, cultures made on the fifth hospital day yielded results essentially identical with those observed in the previous cultures. By the seventh day of hospitalization and treatment by drugs with a broad antimicrobial spectrum, the general condition of the eye seemed to be no better, but possibly worse. Urinalysis at this time revealed a specific gravity of 1.014, with no evidence of reducing sugars, but with a slightly positive test for albumin. Occasional white blood cells, erythrocytes, and casts were noted in the microscopic examination. On the 7th to the 10th day injections of typhoid and paratyphoid vaccine were administered as a means of fever therapy, but no improvement was noted. Corneal scrapings were cultured again, and the growth was not significantly different from that observed previously. Owing to the failure of medical therapeutic measures, a decision was made to enucleate the eye. The procedure was performed successfully on the 12th hospital day, using anesthesia with thiopental (Pentothal) sodium, tubocurarine chloride U. S. P., and oxygen. Except for considerable bleeding, no complications were encountered. The patient recovered uneventfully, and he was discharged from the hospital on the fourth postoperative day.

MICROBIOLOGIC STUDIES

Corneal scrapings were suspended in a small portion of tryptose broth (approximately 1 ml.), and aliquots of the suspension were cultured on blood-tryptose agar, tryptose broth, and thioglycollate broth, the last medium being included for detecting growth of anaerobic organisms. These cultures were incubated at 37 C. In addition, aliquots of the suspension of corneal scrapings were inoculated on Sabouraud's dextrose agar and incubated at room temperature. Other portions of the suspension were used for preparation of smears, which were stained by a modified Gram method and examined directly in order to make correlations with the results from cultures.

All three specimens (collected on the 1st, 5th, and 10th days of hospitalization) yielded essentially similar findings on microscopic examination of smears and cultures. Gram-positive cocci in irregular small groups and diphtheroids were noted in all the smears, and several hemolytic and nonhemolytic colonies of M. pyogenes var. aureus (staphylococci) and a few colonies of Corynebacterium sp. (diphtheroids) were isolated from the corresponding cultures. Two colonies of a fungus were noted in the first set of cultures, but these were interpreted, erroneously, as probable contaminants. Owing to the facts that there were only two colonies and fungi were not noted in the first smears, the organisms were discarded without having been identified specifically. However, when the same type of growth was noted in the second and third sets of cultures and occasional hyphal fragments were observed in the direct smears, transplants were made for further study and identification.

Although the fungus could be isolated on blood-tryptose agar plates incubated at 37 C., the colonies were relatively small and flat, developed more slowly, and produced only slight aerial growth. More characteristic growth occurred on Sabouraud's dextrose agar incubated at room temperature. Colonies attained diameters of 2 to 8 mm. within three to five days after inoculation. They increased in size fairly rapidly, ranging from 30 to 40 mm. in diameter in 14 to 16 days. Aerial hyphae developed early in the cycle, producing a velvet-like, white colony. By the seventh or eighth day of growth, the white aerial mycelium was fairly abundant, and the colony was fluffy and cotton-like. Shortly thereafter the mycelium turned gray, and finally to a light tan, particularly in the more central portion of the colony. Microscopic examination revealed hyphae which were sparingly septate and averaged approximately 4μ to 6μ in width. Preparations made from velvet-like and fluffy white colonies revealed numerous relatively long and slender conidiophores, each of which terminated in a single ovoid conidium, approximately 10μ to 14μ in the longer axis and 6μ to 10μ in the shorter axis. Similar conidia were noted also on shorter, stump-like conidiophores devel-

oped laterally from the hyphae in the mycelium mass. Terminal, lateral, and intercalary chlamydospores were relatively rare in younger cultures on Sabouraud's dextrose agar, but were fairly abundant in the older, pigmented colonies, especially those developed on corn meal agar. None of the cultures revealed evidence of sexual structures (i. e., ascocarp and/or asci with ascospores), and the fungus was identified as M. apiospermum.*

PATHOLOGIC STUDIES

The enucleated eye was not unusual in shape, but it seemed tenser and slightly larger than the average, the axis oculi measuring 28 mm. In general the sclera was gray-white, smooth, and glistening, but the antero-inferior portion was slightly rough and speckled with tiny red-brown foci. The entire corneal surface was defective and rough, presenting as irregular, confluent patches of opaque gray-yellow, slightly shaggy material. Similar material was found in the inferior half of the anterior chamber. The crystalline lens was of the usual biconvex shape, approximately 10 by 5 mm. in size, and its transparency seemed unimpaired. Examination of the vitreous humor, head of the optic nerve, and other structures revealed no gross abnormalities.

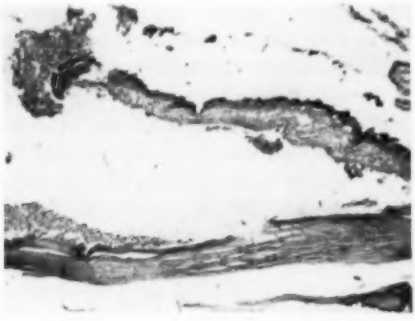

Fig. 1.—Portion of cornea (lower part of field), anterior chamber (middle of field), and iris and ciliary body (upper part of field). Fibrinopurulent exudate is adherent to the inner portion of the degenerated and fragmented cornea. Similar exudate is adherent to the iris, and there is infiltration of inflammatory cells in the muscle. Reduced ⅜ from magnification of approximately × 30.

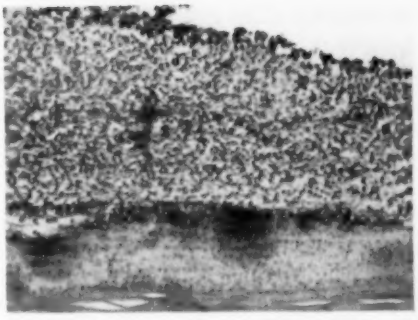

Fig. 2.—Low-power view of sclerocorneal region adjacent to the iridial angle. The exudate consists of polymorphonuclear leucocytes and mononuclear macrophages enmeshed within fine and coarse strands of fibrin. The epithelial cells of the sclera are involved in profound degenerative changes. Reduced ⅜ from magnification of approximately × 100.

Paraffin sections were stained with hematoxylin and eosin and by MacCallum's modification of the Goodpasture-Gram technique. Microscopic examination revealed that the external layer of corneal epithelial cells and the underlying elastic lamina were denuded, and that a thin pseudomembrane of fibrinopurulent exudate was in direct contact with portions of the substantia propria of the cornea. Portions of the substantia propria were degenerated and fragmented. The anterior chamber was partially filled with exudate, which was adherent to the internal epithelial layer of the sclerocorneal junction

Fig. 3.—Oil-immersion view of a portion of the exudate illustrated in Figure 2. Note the hyphae and ovoid conidia, which are morphologically characteristic of similar structures in cultures of M. apiospermum. Reduced ⅜ from magnification of approximately × 1000.

* Dr. Norman F. Conant, Duke University School of Medicine, studied one of the cultures and made a confirmatory identification.

and extended along the inner portion of the cornea almost to the vertex corneae (Fig. 1). The exudate consisted chiefly of polymorphonuclear leucocytes with numerous mononuclear macrophages, enmeshed within an irregular network of fine and coarse strands of fibrin (Fig. 2). Polymorphonuclear leucocytes and mononuclear macrophages were scattered diffusely and in small aggregates throughout the pectinate ligament, the spaces of the iridial angle, the ciliary body, and the iris. In several areas the exudate lying free in the anterior chamber, and that enmeshed within the connective tissue of the iridial angle, contained relatively long and short fragments of septate fungal hyphae and ovoid conidia (Fig. 3). These structures were morphologically characteristic of those observed in cultures of M. apiospermum. Microscopic colonies, or mycotic "granules," were not observed. Gram stains of the histologic sections also revealed several Gram-positive cocci scattered diffusely throughout the exudate.

COMMENT

The medical literature contains many reports concerning infection of the eyelids and conjunctiva, the sclera and cornea, and certain intraocular structures associated with fungi and fungus-like higher bacteria. Although completely satisfactory data are not available in several of the papers, the following organisms have been incriminated as primary causal agents or secondary invaders of considerable importance: Histoplasma capsulatum[1]; Coccidioides immitis[2]; Blastomyces dermatitidis†; Cryptococcus neoformans (Torula)[5]; Sporotrichum Schenckii‡; Candida albicans (Monilia)[8]; "chromoblastomyces"[9]; Oospora[10]; Glenospora graphii[11]; Cephalosporium[12]; Mucor[13]; Rhinosporidium Seeberi,§ and Actinomyces, Streptothrix, and Nocardia.‖ The references cited are not to be regarded as complete, but are merely representative papers that report instances in which different fungi and fungus-like higher bacteria involved the eye or its accessory structures. We believe this paper records the first instance in which M. apiospermum was incriminated as a causal agent or significant secondary invader in a corneal ulcer which progressed to involve the anterior chamber and associated intraocular structures.

M. apiospermum is one of the fungi imperfecti, representing the asexual (or imperfect) phase of one of the Ascomycetes, Allescheria Boydii.¶ Most of the strains isolated from human lesions do not develop sexual spores (ascospores) and are classified as Monosporium species. These organisms are members of a heterogeneous group of fungi which sometimes cause disease in man, known as maduromycosis, or mycetoma.# This clinical entity is a chronic infection affecting the feet usually, but other parts may be involved, with the development of tumor-like masses of granulomatous inflammation and draining sinuses. The disease has been encountered in many parts of the world, including several regions in the United States, where it is more prevalent in the South. The vast majority of these infections occur in men who are farmers, in the third and fourth decades of life, and the relatively few women who contract the disease are usually farm dwellers. Very often there is a history of relatively minor injury, such as a scratch or puncture of the skin by a splinter, especially in persons who go barefooted.

The fungi which cause mycetomas in man are apparently widely disseminated in nature, and most of them are saprophytic forms which may persist on plants, decaying vegetation, and in soil. For example, M. apiospermum has been isolated from samples of soil. As compared with many other infectious agents, this fungus would not be regarded as a good example of a virulent or-

† References 3 and 4.

‡ References 6 and 7.

§ References 14 and 15.

‖ References 4 and 16.

¶ References 16 and 17.

Certain species of Glenospora, Cephalosporium, Phialophora, Indiella, Madurella, and Aspergillus, also, have been incriminated as causal agents of this disease. As noted above, some of these have occurred in ophthalmic infections as well.

ganism. Apparently, numerous human beings may come in contact with it almost constantly, but it causes disease in man relatively rarely. Man must be endowed with some degree of natural resistance, perhaps dependent largely on the skin and mucous membranes functioning as mechanical and/or physiologic barriers. Under certain conditions, however, natural resistance is thwarted, for example, by an injury, and the fungus manages to gain entry to underlying, relatively more susceptible tissues. Here it usually produces an insidious, slowly "smoldering," long-lasting infection in the host, with little or no tendency to disseminate to distant parts.

The exact source of the infection in this patient was not determined, nor did questioning reveal any significant clue regarding the mode by which the Monosporium was transmitted to the eye. However, one should emphasize (1) that the organism is probably disseminated widely in nature, and (2) that the patient was a middle-aged man, actively engaged in farm work. Although there was no knowledge of suffering an injury to the left eye prior to the onset of the corneal ulcer, it seems reasonable to postulate that he may have had an injury which he did not remember or recognize as such. A defect in the corneal epithelium probably provided an excellent portal of entry through which the Monosporium and bacteria invaded internal structures of the eye.

The experience with this patient, and most of that recorded in the literature, indicate that the sulfonamide drugs and antibiotics would not be expected to have specific fungicidal or fungistatic activity. However, these substances may help to control concomitant bacterial infection. If the eye is extensively involved by Monosporium or similar organisms, enucleation would seem to be the procedure of choice in attempting to obliterate the disease.

SUMMARY

The clinical, microbiologic, and pathologic findings in a patient with corneal ulcer, hypopyon, and iridocyclitis are presented. M. apiospermum was cultured from the exudate, and morphologically characteristic fungous structures were demonstrated in histologic sections of the enucleated eye. This case is believed to be the first reported instance in which corneal ulcer and intraocular infection were associated with a species of Monosporium. Sulfonamide drugs and antibiotics were not effective in controlling the infection.

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Clinical Significance of Some Entoptic Phenomena

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Entoptic phenomena are, to the average ophthalmologist, items of physiologic curiosity rather than useful clinical tools. Scheerer's phenomenon, which renders red blood cells circulating in the paramacular region visible, and Haidinger's brushes, which test the integrity of the nerve fibers of Henle's layer, are two of the entoptic phenomena which have advanced from experimental investigation to clinical application. They have proved to be of considerable practical importance, and it is unfortunate that they have not gained the popularity they deserve. We have applied these phenomena to to the study of several patients at the New York Eye and Ear Infirmary and have endeavored to analyze and interpret the results.

SCHEERER'S PHENOMENON

In one of his fundamental articles, Scheerer states that more than a dozen authors, among whom are Helmholtz and Purkinje, have described the phenomenon now known as Scheerer's phenomenon. Nearly all of them made their observation by just looking at the sky, or by looking at a snowfield with a blue glass, and did not attach much importance to this observation. Fortin, in 1901, was the first to employ an instrument for this purpose; he used a mercury vapor lamp with a condensing lens. Scheerer used a Zeiss arc lamp and two Uviol glass filters with a wave length of 3500 to 4500 A., and then two condensing lenses. In order to narrow the field of observation, he used two lenses, the first with a diameter of 4.5 cm. and the second with a diameter of 2.5 cm. With this arrangement the patient sees a brightly illuminated field of a light blue color limited to the macular and paramacular region.

There is no danger to the retina or to the conjunctiva. In the original apparatus, which used an arc lamp, an after-image of a light yellow-green color was present, but in our arrangement no after-image is present and any other examination can be carried out, even visual acuity determination. The present study was carried out with a standard projection apparatus, using a Uviol glass filter and a condensing lens system.*

As soon as the patient begins to look into the lighted field, he sees the flying corpuscles. After a few seconds they become even clearer —only after several minutes will fatigue set in and blur the picture. The corpuscles fly apparently without any rule in all directions, but very soon it becomes clear that there are some principal directions that are constantly followed and that in the main are radial to the macula, and that there are other paths that skirt the macula. If one pays attention only to the brightest corpuscles, one will find in a normal field about 20 to 30 which appear suddenly at a margin of the field or at any place in the field with a sudden jerk. They move along a straight or a curved line with diminishing velocity, and they then disappear just as suddenly as they appear; sometimes they seem to hesitate until they receive a new push, then disappear abruptly. The length of their path is on an average about half the diameter of the whole illuminated field. These paths seem to be constant.

Paper read at the Annual Alumni Spring Meeting, New York Eye and Ear Infirmary, April 19, 1954.

* In the course of our research we have developed a completely different and better apparatus. It will be described in detail in a later publication.

The sudden acceleration is synchronous with the systole, i. e., the dilatation of arteries, but is slightly retarded in relation to the radial pulse. All the corpuscles move at the same time, thus giving proof that they are located in the arterial part of the vessel system. The luminous points are always seen in Indian file, never two together. From a comparison of the paths of the red blood cells and the figure of Purkinje, one comes to the conclusion that these red blood cells are in the retinal arterioles. The visibility does not depend on refractive status or visual acuity.

In performance of the examination, the patient is seated and the head placed in a head rest. The light is focused on the pupillary area. The patient is asked to look into the center of the light source and to observe the presence or absence of moving particles. He is asked to fix in the center of the light, where there are no particles. This area is called Maxwell's spot and corresponds to the foveal region. These moving particles are red blood cells. There are various interpretations of the mechanism of production of the phenomenon, and they can be summarized as follows: (1) total internal reflection of the short-wave-length light, which takes place in the red blood cells; (2) fluorescence of hemoglobin with this wave length, and (3) the unusual direction of the beams of light which come to a focus in the pupil and reach the retina at a more divergent angle than the usual beams, thus stimulating a greater number of rods and cones.

The relatively small number of luminous points have led some observers to believe that they are not red but white blood cells. Adler gives a comprehensive description of the problem as follows:

> To account for the small number of spots, it has been suggested that the red corpuscles overlap one another in a capillary, and therefore cast a continuous shadow on the retina, but when a white cell is present among the red cells, this does not absorb the blue light, having no hemoglobin, and produces a rift in the shadow figure. This rift corresponds to what is seen as a fine bright moving point. Thus, one sees the white corpuscles by the contrast with the red corpuscles and sees them best in light which casts the best shadow, that is, makes the greatest contrast. Since red light passes almost equally well through both erythrocytes and leucocytes, a contrast does not appear.

At the present time it cannot be said which of these theories is correct. There can be scarcely any doubt that the phenomenon is connected intimately with the circulation of the blood.

The following responses are possible:

1. The patient may report 20 to 25 cells with a pulsating motion—this is a normal response.

2. The patient may report (*a*) fewer cells in one eye than in the other, (*b*) corpuscles in uniform motion, or (*c*) a decreased number of cells in one sector. These are abnormal responses.

3. The patient may report no cells—the most abnormal response of the three.

The Scheerer phenomenon is not a difficult one to perceive; it requires only some observation and no great amount of intelligence. It requires far less power of concentration than a visual field determination (Figs. 1, 2, and 3).

The phenomenon can be modified by the action of drugs, as shown by Fischer, who on his own eye proved that miotics, mydriatics, and other drugs affect Scheerer's phenomenon. Pilocarpine and physostigmine cause Maxwell's spot to increase, and fewer red cells are visible. Amyl nitrite slows down the speed of motion of the red blood cells. Homatropine and atropine cause Maxwell's spot to become smaller and more red blood cells to become visible. Nagel was the first to notice that pressure on the sclera increased the number of red blood cells. Vasopressors and vasodilators also have an effect on Scheerer's phenomenon, although this effect is not widely known, and will be the subject of further investigation.

Horniker, who devoted a lifetime to the study of this phenomenon, reached the following conclusion: In a healthy eye uniform motion is always a sign of a vasoneurosis, i. e., a spastic contraction of the retinal arterioles. Diseases of the posterior pole change the type of the movement.

In old retinitis, the movement is also uniform. In all cases of arteriosclerotic changes

Fig. 1.—Normal eye.

of the retinal blood vessels, uniform motion is present a long time before any ophthalmoscopic changes are visible, in contradistinction to diabetes, in which the motion is always a pulsating one.

In incomplete occlusion of the central retinal artery, the motion is uniform, not only in the affected eye but also in the other eye, proving that in such cases there is a general predisposition to this disease.

Uniform current is also found in all cases of chronic simple glaucoma, a finding which should be interpreted as another sign of vasoneurosis in such patients, although one cannot deny that the increased intraocular pressure may play a role. Complete absence of visible motion can be observed in very thick opacities of the media.

The disease which can be discovered by this study is central angiospastic retinopathy. Horniker called it central angiospastic retinitis and attributed the origin to vasomotor instability, but Gifford and Marquardt reviewed the subject and stressed the absence of an inflammatory element, calling the disease central angiospastic retinopathy. Horniker summarized his findings in the following points:

1. Especially important is the nature of onset of the diminished visual acuity. It almost always has a sudden onset, the condition gradually worsening over a period of hours or days. The diminution is described as a veil or spot over the eye that is constant with respect to the eye. Some describe the appearance as that of looking through "hot air." Some of our patients noticed minification of objects. The onset was noted by some to be triggered by psychic disturbances, strong emotions, and exposure to cold and to very bright light.

Fig. 3.—Quadrantic angiospasm.

Fig. 2.—Diffuse macular angiospasm.

2. There is a marked discrepancy between subjective complaints and the visual acuity. In many cases the vision was hardly disturbed, and the loss was of no more than one or two lines on the chart.

3. In all cases the affection was unilateral, and there was a marked preference for males over females.

4. The age group in which the disease is most prevalent is 32 to 45, and the right eye seems to be more commonly affected than the left.

5. Findings with the ordinary ophthalmoscope are nearly always negative. It is with red-free light that one can find extremely minute fundus changes. Only with this method (red-free ophthalmoscopy) is it possible to observe minimal hemorrhages and edema. The first changes to disappear are macular edema, and then the pinpoint hemorrhages, which may persist for months. The visual field does not always reveal a scotoma, even when there is pathology with the red-free light.

All patients that Horniker observed had a complete recovery, but about one-half had a relapse. Horniker concluded the only pathological process that can explain the phenomena observed is an angiospasm. The angiospasm may or may not be a forerunner of essential hypertension, and the spasm must be localized to the capillaries or precapillary arterioles.

Vasoneurosis, which is the basis of central angiospastic retinopathy, is evidenced by bronchial asthma, spastic constipation, mucous colitis, hyperchlorhydria, urticaria, state of deep mental depression, angiospastic crisis (such as migraine and scintillating scotomas), intermittent claudication, angina pectoris, vasomotor rhinitis, and erythema and eczemas.

Occasional factors that may enter the picture are excessive smoking and the menopause. Gifford and Marquardt correlated the occurrence of central angiospastic retinopathy with other evidences of peripheral vascular disease. They felt that the correlation between the two was a close one. Because of the transient attacks, the complete or nearly complete recovery, the ophthalmoscopic evidence of edema during the attacks, and perhaps slight atrophic changes afterward, the predominant involvement of the macula, with its peculiarly vulnerable blood supply, and the absence of congestion or precipitates in the vitreous, they also believed that central angiospastic retinopathy was most certainly a vascular disease.

HAIDINGER BRUSHES

Haidinger brushes have been known for some time but have found clinical application only recently, as a result of the work of Goldschmidt, who devised a simple instrument that allows a quick examination of the macular function. The phenomenon appears to be due to the polarization of light by Henle's fiber layer.

Fig. 4.—Haidinger's brushes.

In Goldschmidt's apparatus, Haidinger's brushes may be compared to a rotating airplane propeller, a pinwheel, or a bundle of hay tied in the middle and rotating around the center (Fig. 4).

This sign is even easier to recognize than Scheerer's phenomenon and requires no special training in its observation. The conclusion reached is that all kinds of ocular anomalies and diseases of the eye in which there is participation of the macula lutea, especially Henle's fiber layer, can be detected in the early stages of the disease.

REPORT OF CASES

CASE 1.—A 37-year-old Negro complained of gradual blurring of vision in the right eye for two

Patient	Age	Sex	Vision	Fundus	Scheerer's, No. RBC	Haidinger's Brushes	Treatment	Final Vision	Fundus	Scheerer's, No. RBC	Haidinger's Brushes
M. H.	37	M	R 20/50 L 20/20	Edema of macula O. D.	R None L 18-20	.....	I. V. and oral nicotinic acid	R 20/20—2 L 20/20	Edema gone	R 20 L 20	....
T. B.	26	M	R 20/30—1 L 20/40+2	Edema of macula O. S.	R 20 L 12-15	....	Nicotinic acid	R 20/20—3 L 20/30+1	Less edema	R 20 L 20	....
S. S.	34	M	R 20/30+3 L 20/20	? Hazy macula O. D.	R 1-2 L 15-20	....	Nicotinic acid		No follow-up		
F. M.	40	M	R 20/25+3 L 20/15	Edema of macula O. D.	R 10-12; slow L 35-40; fast	....	I. V. typhoid vaccine and nicotinic acid	R 20-25 RBC L 35-40 RBC	Edema gone	....	....
J. F.	15	F	R 20/20 L 20/2000	Edema and exudates of macula O. S.	R 100 L None	R Seen L Not seen	Nicotinic acid and antibiotics	R 20/30 L 20/30	Edema gone but slight pigment dispersion	R 60 L 30	R Seen L Seen
H. G.	55	M	R 20/20 L 20/20	Negative	R 25 L 15-18	....	Nicotinic acid	R 20/20 L 20/20	Negative	R 25 L 25	....
A. P.	50	M	R 20/50 L 20/20	Loss of foveal reflex O. D.	R None L 10-15	R Not seen L Seen	Nicotinic acid and Paveril	R 20/40+3 L 20/20	No change	R 6 L 20-25	R Seen L Seen
M. L.	7	M	R 20/20 L HM	Macular hemorrhage O. S.	R 40 L None	R Seen L Not seen	.....		No follow-up		
S. B.	40	M	R 20/20 L 20/20—	Negative	R 35-40 L None	....	Nicotinic acid		No follow-up		
A. B.	45	M	R 20/200 L 20/20	Macular edema and flat retinal detachment O. D.	R None L 20-25	R Not seen L Seen	.....		No follow-up		
S. T.	34	M	R 20/20 L 20/30—3	? Edema of macula O. S.	R 20-40 L None	R Seen L Seen	Nicotinic acid	R 20/20+ L 20/30+	No change	R 25 L None	R Seen L Seen
D. P.	26	M	R 20/20+ L 20/20+	Chorioretinitis near disc O. S.	R 10-15 L 3	R Seen L Seen	Cortisone		No follow-up		
R. S.	31	M	R 20/30 L 20/40	Punctate highlights in macula O. S.	R 20 L None	R Seen L Seen	Nicotinic acid		No follow-up		
J. P.	45	M	L 20/30	Small hemorrhage of macula O. S.	L 5-6	L Not seen	Bed rest and pinhole glasses	L 20/30	No change	L 12	L Seen
B. L.	32	M	R 20/20 L 20/30	Negative	R 20-25 L None	....	Antihistamines	R 20/20 L 20/20	Negative	R 20-25 L 20	....
I. S.	39	F	R 20/40 L 20/20	Sheathing and temporal pallor of disc O. D.	R None L 20	R Not seen L Seen	Nicotinic acid; antihistamines	R 20/20 L 20/20	No change	R 2-3 L 20	R Seen L Seen
D. B.	53	M	R 20/30 L 20/40	Edema of macula O. S.	R 15-20 L None	R Seen L Not seen	Acetazoleamine and nicotinic acid	R 20/20—1 L 20/20—1	Less edema	R 15-20 L None	R Seen L Seen
L. W.	40	F	R 20/20—3 L 20/20	? Edema of macula O. D.	R 10 L 15	R Not seen L Seen	Dioxyline (Paveril)	R 20/20—1 L 20/20	No change	R 15 L 15	R Seen L Seen
A. S.	..	M	R 20/50 L 20/30	Edema of macula O. D. following blow to eye	R 10 L 100	R Not seen L Seen	Nicotinic acid		No follow-up		
M. H.	55	M	R 20/200 L 20/20	Branch occlusion of artery above macula O. D.	R 20 L 50	R Seen L Seen	Trypsin (Parenzyme)		No follow-up		

days. The fundus showed only macular edema. Vision was 20/50 in the right eye and 20/20 in the left eye. Scheerer's phenomenon revealed no cells in the right eye but 18 to 20 red blood cells in the left eye. Haidinger's brushes were not seen by the right eye but were seen by the left eye. The patient was given intravenous nicotinic acid on two occasions during the early course of the disease, with the response in a few minutes of an increase in red cells, of from 0 to 6 in the right eye, and of from 20 to 25 in the left eye, indicating that nicotinic acid has a definite vasodilator action on the retinal precapillary arterioles and capillaries.

CASE 2.—A 53-year-old white man complained of the left eye being "covered by a shadow." The fundus showed macular edema. Vision was 20/30 in the right eye and 20/40 in the left eye. Scheerer's phenomenon revealed 15 to 20 red cells in the right eye and none in the left eye. Haidinger's brushes were seen by the right eye but not by the left eye. Treatment with acetazoleamide (Diamox) and nicotinic acid was begun, and at the last examination the vision was almost 20/20 in each eye. Scheerer's phenomenon showed 15 to 20 red cells in the right eye but still no red cells in the left eye. Haidinger's brushes were seen with each eye, indicating that the brushes are a less sensitive test, macular edema being still present at this stage.

CASE 3.—A 58-year-old white man complained of blurred vision in the right eye and spots before each eye. Fundus examination showed punctate highlights in the macular region of both eyes and no macular reflex in the right eye. Vision was 20/50 in the right eye and 20/20 in the left eye. Scheerer's phenomenon revealed no cells in the right eye and 10 to 15 cells in the left eye. Haidinger's brushes were not seen by the right eye but were seen with the left. At the last examination, the vision had improved to 20/40+3, with the presence of 6 red cells moving slowly and with uniform motion. Haidinger's brushes were seen by the right eye, but the fundus showed no change at this stage.

CASE 4.—A 34-year-old white man complained of "dark vision" and objects appearing smaller with the left eye, of two weeks' duration. Fundus examination showed punctate highlights around the macula of the left eye. Vision was 20/20 in the right eye and 20/30+3 in the left eye. Scheerer's phenomenon was normal in the right eye but showed no cells in the left eye, while Haidinger's brushes could be seen with both eyes.

CASE 5.—A 45-year-old ophthalmologist stated that he noticed one day with amazement that all the patients whom he examined with the ophthalmoscope had a nuclear cataract of the left eye. Late that evening he found that the brown ring he was seeing was his property, and not the patient's. His fundus was negative, and vision was 20/20 in each eye, although slightly blurred in the left. Scheerer's phenomenon was normal in the right eye, but no red cells could be seen in the left eye. Haidinger's brushes were seen with both eyes.

COMMENT

The cases we have studied in this brief survey confirm the value of entoptic phenomena in the interpretation of obscure clinical cases in which the lack or paucity of ophthalmoscopic findings make a definite diagnosis impossible. Their value is enhanced by the fact that entoptic phenomena always appear before definite ophthalmoscopic evidence can be noted. In angiospasm per se, and before an observable edema is present, the patient will show an altered Scheerer's phenomenon. As compared with Haidinger brushes, Scheerer's phenomenon is a more sensitive and reliable test. We have in our series a few patients with definite macular changes, and yet they were perfectly able to tell the direction of rotation of the brushes. The Haidinger brushes seem to be a grosser test than Scheerer's phenomenon but are very useful in following the progress of the condition, since the Hiadinger brushes may revert to normal before Scheerer's phenomenon does, as proved by Case 3.

It is our conviction that angiospasm of a subclinical degree is much more frequent than is generally realized. We have had several patients, not included in our presentation, with vague but persistent complaints, but with no objective findings, who when tested with this method had a definite positive vasal sign (Scheerer). These patients heretofore would be diagnosed as neurotic and sent home with a few words of reassurance. The prescription of a vasodilator relieved their symptoms in a few days.

As we hinted before, there is little ophthalmoscopic evidence for the diagnosis of this disease. The outstanding feature of the fundus is macular edema.

There are three main concepts concerning the pathogenesis of macular edema. They are all based upon interpretation of clinical facts, although the ophthalmoscopic appearance does not vary from type to type. This disparity of opinion is probably due chiefly

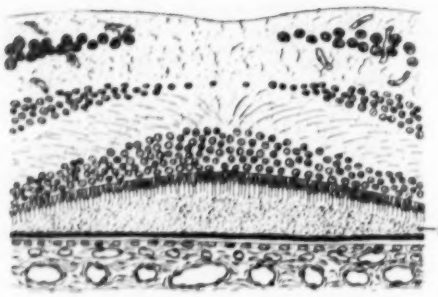


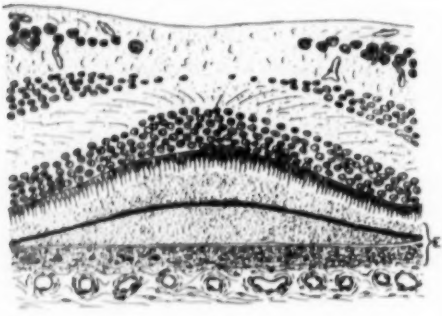
Fig. 5.—Schematic illustration of idiopathic flat detachment of the macula, showing the accumulation of fluid between the pigment epithelium and the layer of rods and cones.

to the lack of histological evidence permitting one to determine with finality the nature of the underlying process.

We have tried to schematize the three principal interpretations, which are (1) the theory of flat retinal detachment (Walsh and Sloan; Fig. 5), (2) the theory of choroidosis centralis serosa (Duggan; Fig. 6), and (3) the theory of central angiospastic retinopathy (Scheerer; Horniker; Gifford and Marquardt; Fig. 7).

According to Walsh and Sloan, the accumulation of fluid is behind the retina, and the cleavage, if it is a real detachment, must be postulated to lie between the layer of rods and cones and the pigment epithelium. This opinion is bolstered by the clinical observations of reduplications of the beam of the Friedenwald ophthalmoscope and transient hyperopia. It does not explain the epi-

Fig. 6.—Schematic illustration, showing Duggan's concept of choroidosis centralis serosa, in which the choroidal vessels are narrowed and fluid has accumulated between the choroid and the retina. The small retinal vessels are of normal size.



sodic nature of the disease or why the detachment, when started, does not progress, as is the rule with detachments that are not stopped by surgical intervention.

Duggan,† in describing a new entity (choroidosis centralis serosa), thinks that the reaction is begun by vasospasm of the choriocapillaris, with edema starting there and moving up through the retina. He feels that the pigment changes seen occasionally, especially after many recurrences, would indicate a choroidal rather than a retinal origin. Duggan bases his chief argument on the visual field changes, in which the scotoma for blue is usually larger than that for red and would indicate a choroidal origin, in contradistinction to a retinal lesion, which has a red scotoma larger than the blue. We find

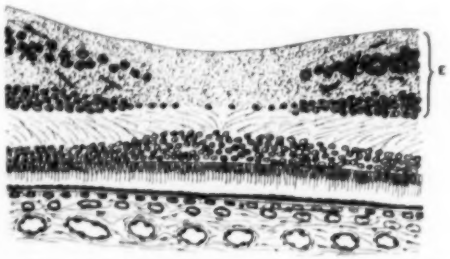


Fig. 7.—Schematic illustration, showing macula in central angiospastic retinopathy. Edema, indicated by deeper stippling, is limited to the area between the inner nuclear layer and the internal limiting membrane. The small retinal vessels are narrowed, but the choroidal vessels are not changed.

it hard to accept his view, because, while a spasm of a terminal artery obviously leads to ischemia and asphyxia of tissues, it is hard to understand how a richly anastomosing network, such as the choriocapillaris is, could lead to these results unless the whole network were affected at the same time.

In our opinion, the known facts as we have pointed them out in the course of this work are consistent with an interpretation of angiospasm of the retinal arterioles. These spasms may start anywhere in the vascular tree but are more frequent in the precapillary arterioles and in the capillaries themselves.

† Duggan, W. F.: Macular Edema, read at the Alumni Meeting of the New York Eye and Ear Infirmary, April 19, 1954.

The localized edema, the vasal signs (Scheerer's phenomena), can be correctly interpreted in the light of this concept. The deep migration of pigment that can be observed in some cases is not proof against this theory. This pigmentary migration appears only after repeated attacks and is obviously due to the spread of edema from the superficial layers of the retina to the pigment epithelium. An effort to bring clarity to this confused problem of macular edema is not merely important for the nomenclature or of purely academic interest. It really involves a correct understanding of the physiopathological process and offers a rational basis for the therapy to be employed.

Theoretically, a central serous choroiditis would cause edema of the overlaying retina without causing any constriction of perimacular blood vessels. It would therefore abolish Haidinger's brushes and leave Scheerer's phenomenon undisturbed. The opposite would happen in genuine central angiospastic retinopathy. For some time at least, angiospasm only would be present, until ischemia would cause edema. Thus, the two phenomena seem to complement each other in the study of macular function, provided they are utilized at the very inception of visual disturbance. Unfortunately, no case came under our observation soon enough to prove this.

SUMMARY AND CONCLUSIONS

The entoptic phenomena (Scheerer's phenomenon and Haidinger's brushes) have been studied and their clinical significance analyzed.

Haidinger's brushes appear or disappear in connection with edema of the macula regardless of retinal circulation.

Scheerer's phenomenon is present, minified, or absent in direct proportion to macular circulation and without regard to macular edema.

A number of cases have been observed and treated and the results tabulated. An attempt has been made to schematize the different types of pathogenic mechanisms of macular edema and to assess the merits of each of them.

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Mucocele of the Eyelid

Report of a Case

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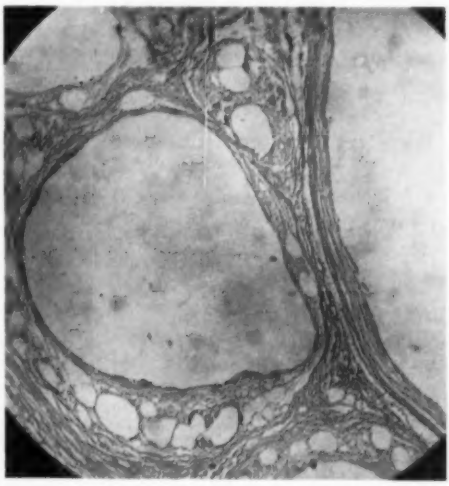
The eyelids are subject to a wide variety of tumefactions. These may arise from structures normally in the lids, by metastasis, or by extension from neighboring tissues. Mucocele of the orbit is not uncommon from the ethmoid sinus. The present report concerns a mucocele in the lateral aspect of the lower eyelid. No reports of this condition could be found in the literature.

REPORT OF CASE

A 22-year-old man was admitted for removal of a mass in the left lower eyelid. One year prior to admission he had sustained an injury to the left side of the face, with fracture of the left maxilla, the orbital floor being depressed. A Caldwell-Luc procedure was done. Several weeks later he became aware of a mass in the left lower lid without pain or redness. The mass gradually increased in size, and for this reason he sought advice.

On examination the right eye was found to be entirely normal. In the left lower lid there was a mass about 10 by 20 mm. in size, involving the lateral two-thirds of the lid. It was of Artgum consistency and was attached to the lateral portion of the inferior orbital margin, extending into the lower lid to within 2 mm. of the lid margin. The overlying skin was not fixed to the mass, and there was no preauricular adenopathy. The left eye was otherwise normal; there was no exophthalmos, and ocular rotations were unaffected.

The tumor was found to be a multiloculated cystic mass firmly adherent to the inferior orbital margin periosteum. During the operation some of the cysts were broken, and clear gelatinous material escaped. Pathological study revealed many cystic spaces lined by a single layer of flattened epithelial cells, showing cilia in some areas. Condensed connective tissue surrounded the cysts (Figure).



Photomicrograph showing cystic nature of the tumor; reduced to ⅝ of mag. × 50.

SUMMARY

An unusual tumor of the lower lid is reported. The tumor apparently originated from mucous membrane of the maxillary antrum, which had been displaced to the orbital margin region at the time of a preceding injury.

62 Basset St.

Effect of Retrobulbar Procaine Injection on Aqueous Humor Dynamics

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The retrobulbar injection of procaine has become almost a standard preoperative procedure in ophthalmology; yet its mode of action on the ocular tension is still unknown. Several recent papers * have described the effect of the retrobulbar injection of anesthetic agents on the intraocular pressure, both in normal and in glaucomatous eyes. Thus far, however, the interest of the research workers has centered mainly on the changes in the intraocular pressure, while other aspects of the aqueous humor dynamics were not considered. It was thought that by employing Grant's tonographic technique,[3] further information might be obtained concerning the mode of action of the retrobulbar injection of anesthetic agents on the intraocular pressure and on other aspects of aqueous humor dynamics. Furthermore, this procedure might throw some light on the neurovascular theory of glaucoma, since the retrobulbar injection effectively blocks all or most of the nerve supply of the eye. Therefore, if the aqueous humor dynamics is under nervous control, it might be significantly affected by this procedure. With this thought in mind, the following study was undertaken.

This study was supported in part by the Alfred P. Sloan Foundation, Inc.

From the Department of Ophthalmology, Columbia University College of Physicians and Surgeons, and the Institute of Ophthalmology, Presbyterian Hospital.

* References 1 and 2.

MATERIALS AND METHODS

This investigation was carried out in the glaucoma department of the Institute of Ophthalmology in New York. The patients had either well-established cases of primary glaucoma or were glaucoma suspects who were found to be normal on further examination. The patients with primary glaucoma had documented histories of chronic simple, open-angle glaucoma followed for several months to several years without operation. In almost all cases the intraocular pressure was elevated at the time the procedure was performed; these patients also showed other manifestations of the disease, such as visual field changes and cupping of the optic disc. In the other group we placed patients with normal eyes; these patients were originally referred to our department because of suspicion of glaucoma, but a period of observation and various provocative tests and clinical examinations have shown that they were free of the disease. Patients with the congestive, narrow-angle, or angle-closure type of glaucoma were not used in the present study because the retrobulbar injection of anesthetic agents affected the size of the pupil, which, in turn, has a considerable influence on the intraocular pressure.

The glaucomatous patients were instructed not to use their miotics for at least 48 hours prior to the test. The solutions used for the retrobulbar injections were 2 cc. of isotonic saline, 2 cc. of 2% procaine HCl, or 2 cc. of 8% procaine HCl, both with or without added hyaluronidase (Hydase), 15 turbidity units per cubic centimeter of solution. Epinephrine was purposely not employed because it is known to affect blood vessels and

thereby might, in turn, influence the intraocular pressure. A 35 mm., 26-gauge needle was used for the retrobulbar injection in a manner described in the previous communication.[4] Tonography, employing Grant's [5] so-called four-minute method, was performed on these eyes 15 minutes prior to the retrobulbar injection. The second tonographic test was carried out approximately 12 minutes after the injection, since previous clinical experience and the work of other investigators have shown that the maximum effect on the intraocular pressure occurs within 10 to 15 minutes after the retrobulbar injection. Other effects of the retrobulbar block, such as the change in exophthalmos, the size of the pupil, and the various motor blocks of the extraocular muscles, were also noticed. However, since the main effort of this investigation concerned itself with the effect of the retrobulbar injection on the aqueous humor dynamics, these other factors were considered only of secondary importance. These observations have already been described in a previous communication.[4]

RESULTS

Ocular tension was measured on 100 eyes both before and after the retrobulbar block, while tonography was performed on 79 of these eyes. As far as the effect on the intraocular pressure is concerned, our results substantiate the findings of Gifford,[1] Snydacker,[2] and other investigators, namely, that in many, but not all cases, the intraocular pressure drops to some extent after the retrobulbar block. This was noticed both in the normal and in the glaucomatous eyes. The hypotony following the injection can be enhanced by pressure on the eye for several minutes, as reported by Atkinson [6] and Chandler † and observed by one of us (F. D. C.) in many cataract cases. Following the injection of isotonic saline solution, with or without hyaluronidase, there was no appreciable change in the intraocular pressure either in the normal or in the glaucomatous cases.

† Chandler, P.: Personal communication to the author.

Table 1 shows the effect of retrobulbar injection of procaine on the tonographic readings in 20 eyes with open-angle glaucoma. In general, it can be seen that the facility of aqueous outflow did not change, while the intraocular pressure dropped somewhat, and this decrease in intraocular pressure was related to a simultaneous decrease in the rate of inflow of aqueous in these eyes. Grant [3] has shown that the rate of flow of aqueous can be calculated by multiplying the facility of aqueous outflow by the intraocular pressure. Therefore, if the facility of outflow does not change, any variation of the intraocular pressure must be related to a corresponding

TABLE 1.—*Effect of Retrobulbar Injection of Procaine Hydrochloride on Aqueous Humor Dynamics of Eyes with Chronic Simple Open-Angle Glaucoma Untreated and Not Operated On**

Eye No.	Before Injection			After Injection			Solution
	C	K	IOP	C	K	IOP	
1	0.11	3.8	37	0.10	2.7	31	2 cc. 2% procaine
2	0.10	4.0	46	0.10	2.9	33	2 cc. 2% procaine
3	0.17	3.9	27	0.17	3.9	27	2 cc. 2% procaine
4	0.06	1.9	37	0.06	2.0	39	2 cc. 2% procaine
5	0.08	2.6	37	0.12	2.2	22	2 cc. 8% procaine
6	0.13	3.9	35	0.12	2.2	22	2 cc. 8% procaine
7	0.10	2.7	32	0.10	2.7	32	2 cc. 8% procaine + Hydase †
8	0.05	1.6	36	0.05	1.2	28	2 cc. 8% procaine + Hydase
9	0.13	4.2	37	0.12	3.0	30	2 cc. 8% procaine + Hydase
10	0.06	2.4	43	0.05	1.8	41	2 cc. 8% procaine + Hydase
11	0.05	1.6	37	0.05	1.3	29	2 cc. 8% procaine + Hydase
12	0.08	2.6	37	0.07	1.7	30	2 cc. 2% procaine + Hydase
13	0.06	2.8	53	0.05	1.7	40	2 cc. 2% procaine + Hydase
14	0.08	2.6	37	0.07	1.8	32	2 cc. 2% procaine + Hydase
15	0.07	2.8	46	0.06	2.0	38	2 cc. 2% procaine + Hydase
16	0.12	3.3	32	0.12	2.6	25	2 cc. 2% procaine + Hydase
17	0.06	1.8	35	0.05	1.2	28	2 cc. 2% procaine + Hydase
18	0.02	0.7	52	0.02	0.8	53	2 cc. 8% procaine + Hydase
19	0.02	1.3	72	0.02	1.2	67	2 cc. 8% procaine + Hydase
20	0.02	1.1	67	0.02	1.0	61	2 cc. 8% procaine + Hydase

* Facility of aqueous outflow (C) expressed as cubic millimeters per minute per millimeter Hg of intraocular pressure; rate of flow of aqueous (K), as cubic millimeters per minute, and intraocular pressure (IOP), as millimeters Hg (Schiøtz).

† Hydase (hyaluronidase) was used in a concentration of 15 turbidity units per cubic centimeter of solution.

TABLE 2.—*Effect of Retrobulbar Injection of Isotonic Saline Solution on Aqueous Humor Dynamics of Eyes with Chronic Simple Open-Angle Glaucoma Untreated and Not Operated On**

Eye No.	Before Injection C	Before Injection K	Before Injection IOP	After Injection C	After Injection K	After Injection IOP	Solution
1	0.10	3.0	35	0.10	3.1	36	2 cc. isotonic saline
2	0.09	1.6	20	0.10	1.8	21	2 cc. isotonic saline
3	0.05	1.5	35	0.05	1.6	37	2 cc. isotonic saline
4	0.10	3.5	40	0.10	3.6	42	2 cc. isotonic saline
5	0.12	3.3	32	0.13	3.9	35	2 cc. isotonic saline
6	0.17	3.9	27	0.19	4.4	27	2 cc. isotonic saline
7	0.05	1.5	35	0.07	2.2	36	2 cc. isotonic saline
8	0.05	1.5	35	0.05	1.6	37	2 cc. isotonic saline
9	0.12	3.5	35	0.13	4.1	37	2 cc. isotonic saline
10	0.19	6.1	37	0.18	5.3	35	2 cc. isotonic saline
11	0.12	3.9	37	0.12	3.7	36	2 cc. isotonic saline + Hydase †
12	0.13	4.2	37	0.12	4.2	40	2 cc. isotonic saline + Hydase
13	0.09	3.6	46	0.09	3.8	48	2 cc. isotonic saline + Hydase
14	0.07	2.1	35	0.08	2.5	36	2 cc. isotonic saline + Hydase
15	0.08	2.6	37	0.07	2.5	40	2 cc. isotonic saline + Hydase
16	0.13	4.2	37	0.14	4.7	39	2 cc. isotonic saline + Hydase
17	0.15	4.5	35	0.17	4.6	32	2 cc. isotonic saline + Hydase
18	0.08	2.7	38	0.09	3.1	40	2 cc. isotonic saline + Hydase

* Facility of aqueous outflow (C) expressed as cubic millimeters per minute per millimeter Hg of intraocular pressure; rate of flow of aqueous (K), as cubic millimeters per minute, and intraocular pressure (IOP), as millimeters Hg (Schiøtz).

† Hydase (hyaluronidase) was used in a concentration of 15 turbidity units per cubic centimeter of solution.

shift in the rate of flow of aqueous. Apparently, this is what takes place in eyes with open-angle glaucoma when procaine is injected retrobulbarly. It was noticed, also, that in seven eyes there was no appreciable change in the tonographic reading following the injection of the anesthetic solution.

Eyes 18, 19, and 20, as shown in Table 1, were cases of absolute glaucoma, due to long-standing open-angle glaucoma. These eyes had no vision at the time of the experiment; their intraocular pressures were elevated, but the eyes were neither congested nor painful. As can be seen from the tonographic results, the facility of aqueous outflow was very low and the total rate of flow was minimal. Therefore, it is not surprising that the retrobulbar injection of procaine had no effect on the aqueous humor dynamics of these eyes; the total rate of flow being already minimal, it could not be further reduced by the procaine and consequently there was practically no effect on the intraocular pressure itself. In a few cases tonography was repeated at 20- to 30-minute intervals after the test; this experiment showed that the changes in the aqueous humor dynamics lasted about one-half to one and one-half hours, an effect which corresponds approximately to that on the optic nerve and the extraocular muscles, as reported previously.[4]

Table 2 demonstrates the effect of retrobulbar injection of isotonic saline solution in 18 eyes with open-angle glaucoma; there was no appreciable effect on the tonographic results following the retrobulbar injection of saline solution. This part of the investigation served as a control to show that the volume of the injection solution does not influence the aqueous humor dynamics of glaucomatous eyes. Table 3 illustrates the effect of the

TABLE 3.—*Effect of Retrobulbar Injection of Procaine Hydrochloride on Aqueous Humor Dynamics of Normal Eyes**

Eye No.	Before Injection C	Before Injection K	Before Injection IOP	After Injection C	After Injection K	After Injection IOP	Solution
1	0.17	3.7	25	0.10	2.3	27	2 cc. 8% procaine
2	0.20	3.2	19	0.17	2.5	17	2 cc. 8% procaine
3	0.24	3.1	14	0.21	2.9	16	2 cc. 8% procaine
4	0.20	3.4	20	0.16	2.5	18	2 cc. 8% procaine
5	0.17	2.7	19	0.16	2.4	17	2 cc. 8% procaine
6	0.15	2.6	20	0.13	2.2	20	2 cc. 8% procaine + Hydase †
7	0.15	2.6	20	0.14	1.8	14	2 cc. 8% procaine + Hydase
8	0.14	2.8	23	0.13	1.9	17	2 cc. 8% procaine + Hydase
9	0.18	3.7	24	0.17	2.3	15	2 cc. 2% procaine + Hydase
10	0.15	3.0	23	0.13	2.2	20	2 cc. 2% procaine + Hydase
11	0.14	2.1	17	0.07	0.9	15	2 cc. 2% procaine + Hydase
12	0.14	1.9	16	0.09	1.4	16	2 cc. 2% procaine + Hydase
13	0.15	3.4	26	0.10	1.8	21	2 cc. 2% procaine + Hydase
14	0.14	3.0	25	0.14	2.8	23	2 cc. 2% procaine + Hydase
15	0.10	2.0	23	0.10	1.9	22	2 cc. 2% procaine + Hydase
16	0.15	3.0	23	0.15	2.9	23	2 cc. 2% procaine
17	0.13	2.6	23	0.13	2.6	23	2 cc. 2% procaine
18	0.10	2.2	25	0.10	2.0	23	2 cc. 2% procaine
19	0.15	3.5	27	0.13	2.3	20	2 cc. 2% procaine
20	0.20	3.4	20	0.17	2.5	17	2 cc. 2% procaine

* Facility of aqueous outflow (C) expressed as cubic millimeters per minute per millimeter Hg of intraocular pressure; rate of flow of aqueous (K), as cubic millimeters per minute, and intraocular pressure (IOP), as millimeters Hg (Schiøtz).

† Hydase (hyaluronidase) was used in a concentration of 15 turbidity units per cubic centimeter of solution.

retrobulbar block on 20 normal eyes. Here the results are more variable. As a rule, after the injection of the anesthetic agent both the facility of aqueous outflow and the rate of flow of aqueous decreased, and simultaneously the intraocular pressure dropped. Again, it can be noticed that in eight eyes there was no appreciable effect following the test. Table 4 shows that the retrobulbar injection of saline in 21 normal eyes had no effect on the tonographic results. It was of interest to note that after the injection of isotonic saline solution (with or without hyaluronidase) a few instances of pupillary dilatation and isolated extraocular muscle paralyses were observed, both in the normal and in the glaucomatous cases. These effects were partial and transient, lasting 5 to 30 minutes only.

TABLE 4.—*Effect of Retrobulbar Injection of Isotonic Saline Solution on Aqueous Humor Dynamics of Normal Eyes**

Eye No.	Before Injection C	Before Injection K	Before Injection IOP	After Injection C	After Injection K	After Injection IOP	Solution
1	0.16	2.2	16	0.14	2.0	16	2 cc. isotonic saline
2	0.21	3.7	21	0.20	3.9	23	2 cc. isotonic saline
3	0.18	2.6	16	0.15	2.1	16	2 cc. isotonic saline
4	0.21	2.7	14	0.19	2.3	13	2 cc. isotonic saline
5	0.21	3.8	22	0.24	4.4	22	2 cc. isotonic saline
6	0.20	3.0	17	0.20	3.3	20	2 cc. isotonic saline
7	0.17	2.7	19	0.17	2.7	19	2 cc. isotonic saline
8	0.18	2.7	17	0.18	2.6	16	2 cc. isotonic saline
9	0.13	2.6	23	0.13	2.6	23	2 cc. isotonic saline
10	0.20	4.9	28	0.20	4.6	27	2 cc. isotonic saline
11	0.22	3.8	20	0.23	3.8	20	2 cc. isotonic saline + Hydase †
12	0.22	3.3	17	0.22	3.4	18	2 cc. isotonic saline + Hydase
13	0.15	2.6	20	0.13	2.4	22	2 cc. isotonic saline + Hydase
14	0.12	2.1	21	0.13	2.4	22	2 cc. isotonic saline + Hydase
15	0.11	1.6	17	0.13	2.0	18	2 cc. isotonic saline + Hydase
16	0.16	2.1	14	0.13	1.8	16	2 cc. isotonic saline + Hydase
17	0.15	2.6	20	0.15	2.7	21	2 cc. isotonic saline + Hydase
18	0.13	2.2	20	0.13	2.4	22	2 cc. isotonic saline + Hydase
19	0.14	3.0	25	0.15	3.5	27	2 cc. isotonic saline + Hydase
20	0.15	3.5	27	0.14	3.0	25	2 cc. isotonic saline + Hydase
21	0.21	4.7	26	0.20	4.6	27	3 cc. isotonic saline + Hydase

* Facility of aqueous outflow (C) expressed as cubic millimeters per minute per millimeter Hg of intraocular pressure; rate of flow of aqueous (K), as cubic millimeters per minute, and intraocular pressure (IOP), as millimeters Hg (Schiøtz).

† Hydase (hyaluronidase) was used in a concentration of 15 turbidity units per cubic centimeter of solution.

COMMENT

The most interesting observation found in this study was that following the retrobulbar injection of an anesthetic agent there was no change in the facility of aqueous outflow, as measured by tonography, in open-angle glaucoma. It was fairly obvious in most of these cases that the retrobulbar injection furnished a good block of both sensory and motor nerves in the orbit. Yet, when these nervous components were anesthetized, there was no change in the facility of aqueous outflow. This fact is interesting because it apparently shows that one of the major characteristics of open-angle glaucoma, namely, the increased resistance to the outflow of aqueous, becomes fixed to the extent that nerve blocks no longer exert any influence.

Previous communications ‡ by one of us (A. de R.) from this department have shown that the facility of aqueous outflow in open-angle glaucoma is a fairly stable factor. At least, it did not seem to show diurnal variations and was not affected by changes in the osmotic pressure of the blood. Thus, it appears that in well-established cases of open-angle glaucoma the resistance to the outflow of aqueous is not influenced by a variety of factors that are known to affect the intraocular pressure itself.

On the other hand, it was noticed that the drop in intraocular pressure that was observed in these cases was related to a corresponding decrease in the total rate of inflow of aqueous through these eyes, as calculated according to Grant's [3] method. Concerning the effect of the anesthetic agent on normal eyes, the results were more variable; the facility of aqueous outflow appeared to be more elastic in these normal eyes, and it did decrease in some of these cases. The effect of isotonic saline solution was negligible in both normal and glaucomatous eyes, showing that the volume of the retrobulbarly injected solution does not influence the tonographic results.

‡ References 7 and 8.

SUMMARY

Retrobulbar injection of procaine in eyes with chronic simple open-angle glaucoma that was untreated and for which operation had not been done did not influence the resistance to the outflow of aqueous, as measured by tonography.

The drop in intraocular pressure observed in these cases, on the other hand, seemed to be related to a simultaneous decrease in the rate of inflow of aqueous through these eyes. In normal eyes, the resistance to the outflow of aqueous seemed more elastic; tonography revealed some changes in the facility of aqueous outflow following the retrobulbar injection of procaine solution.

Retrobulbar injection of isotonic saline solution, in both normal and glaucomatous eyes, had no effect on the tonographic results.

635 W. 165th St. (32).

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Use of Fine Alloy Steel Wire Sutures in Ophthalmic Surgery

Experimental and Clinical Observations

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Following the introduction by Babcock [1] of fine alloy steel wire as suture material in general surgery in 1934, there has been increasing acclaim of its many advantages.[2] It was found by carefully controlled studies that wire sutures produced the least amount of tissue reaction and promoted the most rapid healing of wounds. This effect was noted on or adjacent to mucous surfaces, in plastic operations about the mouth, in the closure of cleft palate, and in numerous other conditions. It was but natural that this suture material should be indicated in ophthalmic procedures, especially since poor wound healing has been considered one of the major causes of postcataract complications. If longer and better approximation of the wound edges were attainable by the use of fine alloy steel wire,* it would seem rewarding enough to test the feasibility of employment of the material in a few ophthalmic procedures.

TECHNICAL DATA

Several types of sutures were prepared for ophthalmological use;† after many trials, we finally selected a suture designated as "Experimental #384." It is a multistrand (twisted, not braided) stainless steel wire suture, 6-0, swaged on to a CE-2 cutting needle, ⅜ circle, double-armed, 9 in. in length. The suture is put up in the usual boilable tube. The Grieshaber needle was tried threaded with the same material but proved unsatisfactory because of needle breakage.

A major difficulty was the irritation from the knots, which were tied in the usual manner. We conceived the idea of clamping a silver bead‡ on to the wire suture. The smallest diameter of the bead which it was possible to manufacture was $^{3}/_{32}$ in., the hole just allowing our curved needle to pass freely. It was found necessary to pass both arms of the suture through the same side of the bead; otherwise there was a tendency for the wound edges to separate. Since these beads are rather hollow, they became quite flat when clamped. Some of our most recent experiments were done with the smallest commercially available lead shot, which were partially slit by ourselves. The shot is held in a needle holder, applied to the suture several inches above the wound, and slid gently down to the wound and clamped. The suture is cut as closely to the bead as possible. This method has given the best wound closure to date.

Rabbits were employed exclusively. Anesthesia consisted of intravenous thiopental (Pentothal), 30 mg./kg., supplemented with tetracaine (Pontocaine) locally and by ether inhalation when necessary. The incision was

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* Hereafter designated "wire suture."

† Dr. G. B. Ayres, Director of Research, Davis & Geck, Inc., helped in the preparation and supplying of all the sutures.

‡ The D. E. Makepeace Co., Attleboro, Mass., prepared the silver beads for us.

made by a special blade prepared from a Gillette Blue Blade. This blade, broken off by forceps, was from 10 to 12 mm. long and from 1.0 to 1.5 mm. wide. After some practice, these blades could be easily duplicated, and each was discarded after being once used. It was held in the Weaver knife blade handle or any small handle equipped with a fine chuck. No scissors or keratome was ever used in making the wound. Iridectomy was not performed. The incision was made in the clear part of the cornea just beyond the limbus, cutting truly perpendicularly to the surface. A drop of fluorscein was instilled to demarcate the incision, which was deepened carefully until aqueous just began to appear. The blade was then reversed and the wound lengthened by cutting from within outward to any length desired. The extreme narrowness of the blade allows great control in keeping the incision always perpendicular. It was felt that this procedure alone lays the groundwork for a successful corneoscleral suture. One of us (D. F.) has used this procedure successfully in one human case.

The incision varied in length from 4 to 6 mm., and either one or two sutures were inserted. Usually the quiet animal received no lid sutures; but the unruly animal had the nictitating membrane sutured to the upper lid, and the lids were closed by three interrupted marginal sutures.

In all, about 50 operations were performed on the 18 eyes of 9 animals. Observations on the eyes operated on and on the controls extended over a period of about two years. One corneal graft operation is not reported because the number of observations were too small, and the procedure is deemed complicated enough to warrant a separate study. Serial sections were cut through the suture areas in both early and late stages of healing.

COMMENT

Soon after these studies were begun, it was quite evident that the traditional methods of handling ophthalmic sutures could not be applied to the wire suture. The new material was springy, and it kinked. This difficulty was somewhat alleviated by using twisted material and shortening the length to 9 in. Too much tension would cause the wire to cut through the tissue postoperatively, and in a bandaged eye corneal abrasions might occur. Loose suture ends, no matter how short, caused conjunctival irritation and discharge. Many general surgeons have adopted the procedure of twisting the suture ends three turns, but in ophthalmic surgery the conditions are quite different. The partially split lead bead appears to be our best solution to the knot problem.

The following variation which we tried was fairly successful: One needle was introduced into the cornea through the wound margin; a double or triple knot was tied on this suture arm and cut very close to the knot. The other needle and suture arm were inserted through the wound margin toward the limbus in the usual way; on closing, this arm has the bead placed on it close to the wound, and the double knot acts as a stop on the cornea. It is almost impossible to pull the knot through the cornea, but the tension on the suture should always be minimal.

The corneal suture may be preplaced or postplaced, as with other sutures. Just enough tension should be exerted to approximate the wound edges, thus allowing for postoperative swelling. A bead pressed too firmly against the cornea caused capillary proliferation and the formation of granulation tissue. We have not seen inversion of the wound edges at any time. As the wound heals, the suture becomes less taut and can be easily removed. Suture scissors are not harmed in cutting the fine wire. A good bite favors the retention of the suture. A bleb of mucus is commonly seen adhering to the bead. This has no significance as to healing. We do not think the lead of the bead has any adverse chemical effect. In using the twisted wire suture, it is important not to cut the knot accidentally, since small particles will be lost in the wound. Thereafter, the eye remains red, and small particles of wire are extruded subconjunctivally over the weeks until all are expelled.

The outstanding quality of the wire suture is its minimal irritation of the corneal tissue. Our pathological studies showed an accumulation of small and large round cells and fibroblasts in the wound area. The base of the iris never showed any cellular reaction. As healing proceeded, these cells became fewer in number, until finally a small star-shaped figure of small round cells remained. We had several rabbits which carried the wire suture and silver bead for over 70 days without any sign of irritation. In our first series of animals, in which the knot was employed, it was frequently difficult to find the suture because the conjunctiva had grown over the area. Sutures buried in the external rectus muscle caused marked irritation and had to be removed after about one week. This was especially true in very thin muscle and when movement caused added irritation. However, several animals which had thicker external rectus muscles tolerated deeply placed wire sutures extremely well.

One patient received two wire sutures for closure of the wound after cataract surgery. A double knot was used, and the ends were cut about 1 mm. long. Postoperative irritation was troublesome, and the sutures had to be removed on the eighth postoperative day. Healing, however, was excellent, and the final correction gave normal vision. The minimal ideal period for good postoperative corneal wound healing, in our opinion, would appear to be about 21 days. If the wire suture could be worn comfortably for this period, one major cause of postoperative failure would be circumvented.

SUMMARY

Some observations on the use of fine alloy steel wire sutures in a few ophthalmic procedures are reported. Certain difficulties have been encountered and remain unsolved. However, the outstanding quality of the wire suture—that of minimal tissue irritation—remains to be exploited by further research by ophthalmic surgeons.

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Supplemental Testosterone and Estrone in Alloxan Diabetes of the Rat

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Conflicting clinical reports * have recently been published concerning the role of androgens and estrogens in diabetic retinopathy. Unfortunately, neither bioassays nor chemical analyses for tissue levels of these hormones are sufficiently accurate to support the endocrine hypotheses involved. Because of the divergent clinical conclusions and the current impassé in obtaining quantitative hormonal assays, a controlled laboratory study has been undertaken in an experimental diabetic animal. Albino rats rendered diabetic by alloxan were used, it being recognized that retinal vascular changes in the rat, as in most experimental diabetic animals, have been produced only with difficulty,† and only in the presence of some additional disturbance or tissue insult. Supplemental estrone was given to one group of diabetic rats in accordance with the hypothesis that this might precipitate additional tissue insult leading to retinopathy. Similarly, testosterone was given to another group on the basis that it might protect against the development of retinopathy.

Initially, an effort was made to adapt the Hotchkiss - McManus - Friedenwald ‡ (periodic acid-Schiff reaction) technique to histologic study of these rat retinas in whole-mount preparation. The intense purple background stain, however, renders this technique unsuitable for rat material. Extensive modifications in tissue preparation and in staining procedure, by both immersion and intravascular techniques, however, failed to yield good definition of the retinal vessels in their smaller divisions.[10]

Our experiments in method indicated that common carotid artery injections of India ink following water perfusion in the intact animal yielded the clearest definition of retinal vascular patterns in whole-mount preparations from the albino rat. Conventional serial sections, however, still offer a most profitable and convenient method for histologic study, particularly since the small size of the rat eye enables an entire globe to be mounted on two slides if the sections are cut at 12μ.

METHOD

Two hundred ten adult albino rats, weighing between 150 and 250 gm., were divided into four groups, containing equal numbers of male and female animals.

1. Control animals kept under the same laboratory conditions as all other animals but not rendered diabetic (10 animals)

2. Diabetic control animals which were alloxanized but received no experimental treatment

3. Experimental animals rendered diabetic with alloxan and treated with an aqueous suspension of

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* References 1 to 3.

† References 4 to 6.

‡ References 7 to 9.

estrone,‖ 5 mg/kg., by subcutaneous injection every four days.

4. Experimental animals rendered diabetic with alloxan and treated with testosterone cyclopentylpropionate¶ in cottonseed oil at a dose of 20 mg/kg., by subcutaneous injection every four weeks.

Animals were maintained on Purina Lab Chow and water ad lib. Diabetes was induced after a 48-hour fast, during which the rats were allowed water ad lib. Nonsterilized 5% solutions of alloxan monohydrate (Eastman Organic Chemicals Dept.) in double-distilled water were given by subcutaneous or intraperitoneal injections at doses of 200 mg/kg. or 175 to 185 mg/kg., respectively, in accordance with the route used. Only freshly prepared alloxan solutions were employed.

Animals were allowed only isotonic saline solution ad lib during the first 48 hours after injection, and they then returned to the standard laboratory diet. Injections of 1 to 2 units of protamine zinc insulin were administered to 69 rats according to clinical indications from the third to the fifth day following alloxan injection. The rat is known to be rather resistant to insulin, and no attempt was made to carry any animal on this type of therapy.

Weekly records of weight were maintained on all animals, and 24-hour urine specimens were collected from each animal at two-week intervals for determination of volume output and total sugar (Hawkins and Van Slyke method).

Of the 200 alloxanized animals, 117, or 58.5%, died in the initial postinjection period of eight days. Of animals surviving the postinjection period, 78.5% became diabetic, and 94.5% of these sustained their disease with rather consistent glycosuria during their experimental lives.

‖ Estrone was supplied as Estrone Lilly through the courtesy of Dr. W. R. Kirtley, of the Medical Department, Eli Lilly & Company, Indianapolis 6.

¶ Testosterone was supplied as Depo-Testosterone Cyclopentylpropionate in oil (25 mg/cc.) through the courtesy of Dr. H. F. Hailman, of The Upjohn Company, Kalamazoo, Mich.

RESULTS

General Observations.—Surviving animals were grouped as short-term survivors, living 8 days to 2 months after alloxanization (63 animals) or as long-term survivors, living 2 to 11 months (22 diabetic animals plus the nondiabetic control animals). The average experimental age of the long-term diabetic survivors was seven and one-half months. No attempt was made to utilize the eyes of short-term surviving animals for histologic study. Eyes from 24 long-term survivors were mounted for study by serial section (hematoxylin and Triosin # stain). Flat mounts of the retina were also made from eyes of several of these animals. Some retinas were lost in early attempts to use the Hotchkiss-McManus staining technique.

Surviving animals frequently developed cataracts in four to eight weeks and generally showed marked weight loss. Twenty-four-hour urine volumes of 70 to 150 cc. (normal is 7 to 14 cc.) and glycosuria of 1.5% to 4.7% were common in most rats. Testicular atrophy was not quantitated but was observed in practically all male diabetic animals.

Long after the development of mature cataracts in both eyes, a few animals were found to lose all apparent reaction to light. These alterations were subsequently found to be associated with uveitis and optic neuritis.

The following tabulation indicates rats which survived for histologic study in the various groups:

Nondiabetic controls	2
Diabetic controls	6
Estrone-supplemented diabetics	9
Testosterone-supplemented diabetics	7

Sex Distribution.—Sex distribution in surviving animals persisted, with an equal number of males and females in each group, just as at the initiation of these studies.

Weight Changes.—The nondiabetic control animals all gained from 150 to 180 gm. during the course of observation. The dia-

Practically identical with eosin Y.

betic control animals lost from 60 to 120 gm. during their experimental life. The estrone-supplemented rats showed distinctly the best weight maintenance among the diabetic groups; some of these animals gained up to 35 gm., and none lost more than 85 gm. The testosterone-supplemented rats were intermediate between the estrone-supplemented and the control diabetic groups, showing weight losses of 0 to 110 gm.

Classification of Histologic Findings.—Eyes of rats surviving for study were basically classified as (*a*) histologically normal eyes, (*b*) eyes showing inflammatory disease, and (*c*) eyes with retinal vascular changes of the early diabetic type.

True capillary microaneurysms and retinitis proliferans were not demonstrated. In diabetic animals from all groups, small hemorrhages were often seen at the outer edge of the inner nuclear layer and the inner portion of the outer plexiform layer. This area is a region of marked capillarity in the rat, as well as in the human eye. Discrete exudates were not found in the outer plexiform layers, but rarely they were seen in the ganglion layers, where occasional hemorrhages were also found. A few areas of questionable, early retinitis proliferans were seen in several older diabetic animals. Considerable care must be used, however, in tracing through serial sections to avoid placing such an interpretation on small vascular loops or knuckles often produced as artifacts by small folds or wrinkles in the surface of the retina.

Some hyalinization of vessel walls was found infrequently in eyes from diabetic animals and also in eyes from nondiabetic control animals which were more than 2 years old.

Inflammatory changes, not specific for diabetes, were found in sections from three rats which had been observed to be totally blind. Edema and round-cell infiltrates were seen in the optic nerves, uvea, and anterior and posterior chambers. Fibrinous debris was found in the vitreous of these eyes. Moderate to intense choroidal congestion was present in eyes from diabetic animals showing inflammatory changes.

The eyes appearing to be histologically normal from 14 of the long-term surviving animals were in practically the same distribution ratio in each of the four groups, within the statistical limitations for samples of this size. The ratio of male to female animals affording histologically normal eyes was also essentially 1:1 in each of the four groups.

SUMMARY AND CONCLUSIONS

The Hotchkiss - McManus - Friedenwald staining technique for demonstration of retinal vascular patterns in whole-mount preparations is not currently adaptable to the albino rat eye because of the intense purple background staining, which obscures the finer divisions of the retinal vessels. India-ink injection preparations appear to produce detailed and consistent demonstrations of retinal vascular patterns in the albino rat. Serial sections with more familiar stains, such as hematoxylin and Triosin, are still of great value in following histologic details through small specimens, as afforded by the rat eye.

No significant differences could be found in the incidence or severity of retinal changes in alloxan diabetic rats of either sex used as controls or in those receiving supplemental estrone or testosterone. Histologically normal eyes were recovered in similar percentages from all groups of diabetic rats in this study. From these findings it is concluded that neither testosterone nor estrone administered in moderately large doses, as specified, over periods of 2 to 11 months significantly affect the histology of the retina in the alloxan diabetic rat.

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News and Comment

SOCIETY NEWS

Ophthalmological Society of Egypt.—The Annual Meeting of the Ophthalmological Society of Egypt will take place at the Memorial Ophthalmic Laboratory, Giza, on Friday and Saturday, March 4 and 5, 1955, at 9 a. m. Medical practitioners, oculists or otherwise, are cordially invited.

South Carolina Society of Ophthalmology and Otolaryngology.—The North Carolina Eye, Ear, Nose and Throat Society and the South Carolina Society of Ophthalmology and Otolaryngology will hold a joint meeting at Columbia, S. C., on Sept. 12, 13, and 14, 1955. Headquarters will be the Columbia Hotel.

The following ophthalmologists will be on the program: Dr. E. W. D. Norton, New York; Dr. Frank Carroll, New York, and Dr. William B. Clark, New Orleans.

An announcement of the three guest otolaryngologists will be made later.

Notched Retractor and Speculum Blades for Ocular Surgery

JOHN P. KEIZER, M.D., Portland, Ore.

In retraction of the lids for ocular surgery, more is involved than exposure of the eye. Generally it is essential for the lids to be held open in such a manner than no pressure is placed on the globe. Also, it is desirable from the point of view of asepsis to shield the operative wound from the lid margins, which are a potential source of infection. To achieve these objectives ophthalmic surgeons have used lid sutures, retractors, or self-retaining speculums, alone or in conjunction with orbicularis akinesia. Each method of retracting the lids has its advantages and disadvantages.

The lids can be retracted effectively by sutures placed in the skin at the palpebral margins; however, this requires infiltration of the lids with a local anesthetic. Some edema and hemorrhage is inevitable. If the procedure is prolonged, the pull of the sutures on the lids may cause the patient considerable discomfort. Finally, these sutures do not permit coverage of the lid margins.

For routine ocular surgery, the use of lid retractors is impractical, because an assistant is required to use both hands to hold them; however, lid retractors are useful during irrigation of the conjunctival sac prior to surgery or for extreme retraction of one lid. The standard Desmarres retractors are so curved that they may slip out when shifted toward the outer canthus. This slip occurs because the lid margins curve back sharply on the lateral side (Fig. 1*a*). The grinding of a simple notch in the blade of the Desmarres retractor eliminates this difficulty. The notch is made just large enough to fit over the lid margin and just deep enough to hold the margin snugly (Fig. 1*b*). The notched retractor can be disengaged simply by rotating the handle. A small model is useful for retracting a conjunctival or Tenon

From the Department of Ophthalmology, the University of Oregon Medical School.

Fig. 1.—(*a*) The standard Desmarres retractor tends to slip out as it is shifted laterally, where the lid curves sharply posterior. (*b*) In contrast, a retractor notched to fit the lid margin becomes more securely engaged.

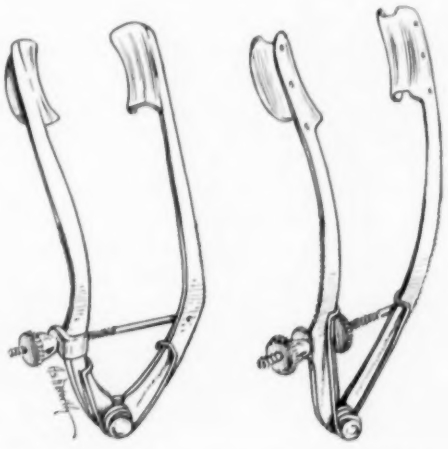


Fig. 2.—(*a*) Lancaster speculum and (*b*) O'Connor-Lancaster speculum with blades to fit the lid margin.

flap in operation on the sclera or extraocular muscles.

Some type of self-retaining speculum is the most commonly used for exposure of the globe in ophthalmic surgery. Many surgeons consider a self-retaining speculum hazardous, for disastrous consequences may result if the speculum suddenly slips out during the course of intraocular surgery. Ideally, therefore, a self-retaining speculum would be one which could be inserted easily but would not slip out even when it was elevated to reduce the pressure of the lids on the globe or to expose the fornices. Such a speculum would have value from the point of view of asepsis if it had a broad solid blade which at least partially covered the glands along the lid margin and the eyelashes. The solid blades of the type used in the Lancaster speculum are an example. The curve of the Lancaster speculum (Fig. 2*a*) is deep enough to permit the insertion of a drape between the blade and the skin of the lid. Roderick O'Connor has improved the Lancaster speculum by widening the blade and incorporating a setscrew inside the arms of the retractor so that, even if akinesia is incomplete, the patient cannot close the speculum by the pressure of his lids. I have found that cutting notches in the margins of the blade of the O'Connor-Lancaster speculum (Fig. 2*b*) permits the lid margin to become so engaged that the security of the speculum actually is increased by shifting the speculum toward the lateral canthus. In contrast, the unmodified O'Connor - Lancaster speculum tends to slide out.

Notching of speculum and the retractor blades can be done easily in a home workshop or by a local mechanic with a hand-grinding tool. The safety and effectiveness of these instruments are increased appreciably by this simple modification.

Histology of Levator Muscle in Congenital and Acquired Ptosis

R. N. BERKE, M.D., Hackensack, N. J.
and
JOSEPH A. C. WADSWORTH, M.D., New York

During the past six years we have studied 116 biopsy specimens of the levator muscle from patients with ptosis. Our purpose has been threefold: first, to ascertain the histological nature of the levator muscle in congenital and acquired ptosis; second, to learn whether the histological structure of the levator in these cases affected the final results of resection of the levator muscle, and, third, to elucidate the cause of congenital ptosis.

REPORTED PATHOLOGICAL FINDINGS IN CONGENITAL PTOSIS

Only a few gross anatomical and histological reports on the structure of the levator muscle in congenital ptosis are available. For example, Heuck [1] (1879) removed post mortem the orbits of an 18-year-old youth with complete congenital ptosis and demonstrated an atrophic levator, only 2 mm. wide, in the right orbit and complete absence of the levator in the left. In addition, both superior rectus muscles were very thin and almost nonexistent. Bach [2] (1895) removed after death large pieces of the levator and extraocular muscles from the orbit of an 18-year-old woman with congenital ptosis. Microscopic study showed marked atrophy and poor development of the levator and the superior rectus muscles. In a case of complete bilateral congenital ptosis, Ahlström [3] (1895) found only a few tendon fibers of the levator in the right upper lid and no trace of this muscle on the left side. Siemerling [4] (1891) studied histologically the two levator muscles and the two third cranial nerves and their nuclei in a case of incomplete left-sided ptosis. He found some degeneration of the left levator muscle, the left third nerve, and both third nerve nuclei and speculated that the ptosis resulted from a lesion in the third nerve nucleus.

Other extraocular muscle anomalies are sometimes associated with congenital ptosis, such as abnormal insertions of the extraocular muscles, bifurcation of the levator muscle, and incomplete separation of the superior rectus and the levator muscles (Wilbrand and Saenger,[5] Posey,[6] Macklin,* Lawford,† Steinheim,[12] Natale [13]).

Aside from these few reports, little is known of the histology of the levator in congenital or acquired ptosis.

GROSS ANATOMY OF LEVATOR MUSCLE

A gross anatomical study of several normal cadaver orbits showed that the striated muscle fibers of the levator muscle run forward from the apex of the orbit to a point about 10 mm. from the upper border of the tarsus (*D*, Fig. 1), where these fibers end and are replaced by two layers of tissue. The upper layer, known as the aponeurosis, inserts into the anterior surface of the tarsus, the adjacent orbicularis muscle, and the overlying skin. The lower layer, known as Müller's upper lid muscle, inserts into the upper edge of the tarsus (area *A*, Fig. 2; Fig. 3).

From the Institute of Ophthalmology of Columbia-Presbyterian Medical Center.

* References 7 through 9.
† References 10 and 11.

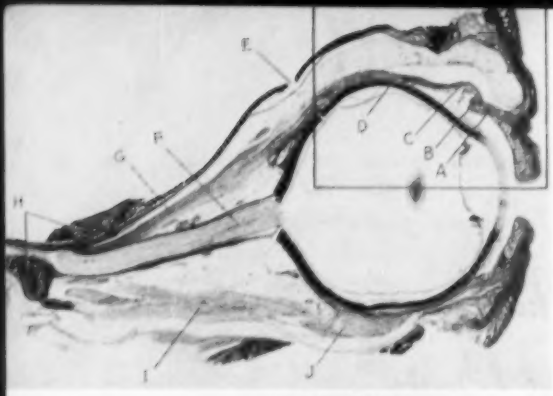


Fig. 1.—Sagittal section of orbit of stillborn.

A, Müller's ligament to tarsus; *B*, Müller's muscle; *C*, tendon of levator palpebrae muscle; *D*, anterior end of striated muscle of levator; *E*, break in periosteum of orbital roof; *F*, central retinal artery in optic nerve; *G*, superior rectus and levator muscles; *H*, bone above and below optic canal; *I*, inferior rectus muscle; *J*, inferior oblique muscle.

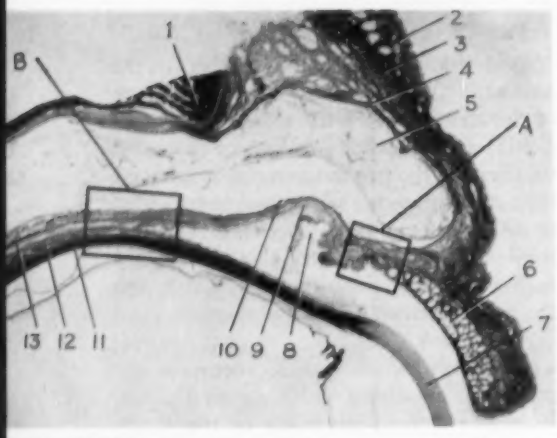


Fig. 2.—Higher-power photomicrograph of rectangular area outlined in Figure 1.

1, superior orbital bony margin; *2*, skin; *3*, orbicularis muscle; *4*, septum orbitale (pushed forward by orbital fat and injected preserving fluid); *5*, orbital fat (pushed forward); *6*, tarsus; *7*, cornea; *8*, upper fornix (displaced forward by preserving fluid); *9*, Müller's smooth muscle; *10*, levator aponeurosis; *11*, sclera; *12*, tendon of superior rectus muscle; *13*, skeletal muscle of levator.

A, area of insertion of Müller's muscle to upper edge of tarsus.

B, area of origin of Müller's muscle and aponeurosis from skeletal muscle fibers of levator.

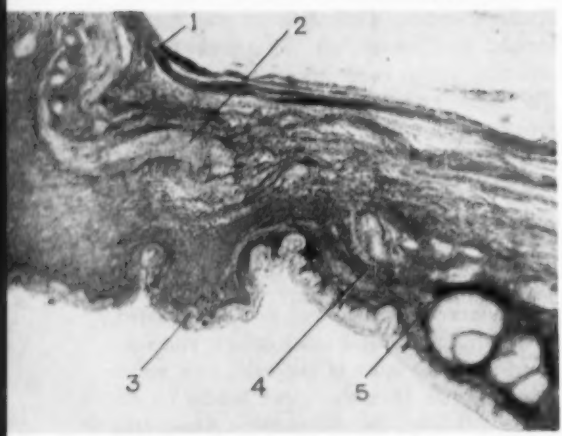


Fig. 3.—High-power magnification of area *A* from Figure 2.

1, levator aponeurosis; *2*, anterior end of Müller's muscle; *3*, conjunctiva of upper fornix; *4*, "tendon" from Müller's muscle (*2*) to tarsus (*5*); *5*, upper edge of tarsus.

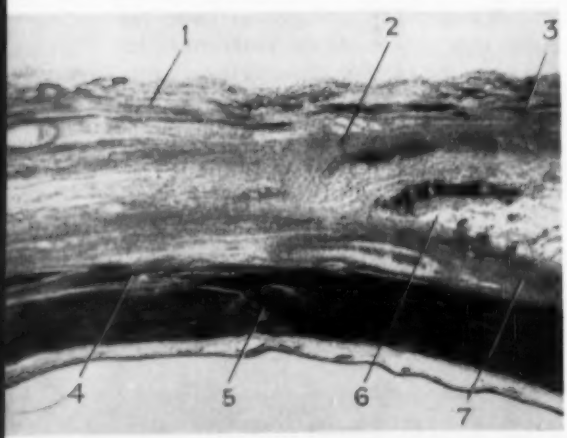


Fig. 4.—High-power view of area *B* from Figure 2.

1, skeletal muscle fibers of the levator; *2*, Müller's muscle (joins levator farther to left); *3*, origin of levator aponeurosis from uppermost skeletal muscle fibers of levator; *4*, tendon of superior rectus muscle at site of insertion to sclera; *5*, sclera; *6*, normal position of upper fornix, which has been displaced forward by injected fluid; *7*, Tenon's capsule.

NORMAL HISTOLOGY OF LEVATOR MUSCLE

In order to familiarize ourselves with the normal histology of the levator and its relationships, we examined several biopsy specimens of cadaver levators histologically. This study was augmented by the examination of sagittal sections of several exenterated orbits from the pathology collections of the Institute of Ophthalmology and from the Surgeon General's Library, Washington, D. C.‡ In addition, we were fortunate to have access to Dr. George M. Smelser's excellent collection of histological sections of the entire orbital contents of a stillborn child, from which the photographs in Figures 1 to 4 were made.§

‡ Through the courtesy of Mrs. Helenor Wilder.

§ Unfortunately, the normal anatomy in these sections is slightly distorted because the septum orbitale, the orbital fat, the upper fornix, and the globe are pushed forward by the preserving fluid injected for fixation of the tissues.

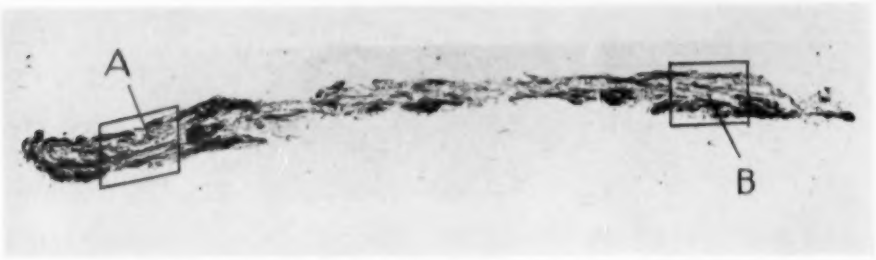


Fig. 5.—Low-power magnification of sagittal section taken from levator muscle excised in a case of acquired ptosis (Table 2).

These histological studies confirmed our description of the gross anatomy of the levator given above, except that Müller's muscle, which seems in gross sections to be inserted directly into the upper edge of the tarsus, actually is separated from the tarsus by a short "tendon," about 1 mm. in length (Fig. 3). The smooth muscle fibers of Müller's muscle are easily identified in the trichrome stain; they extend backward from the tarsus (*A*, Fig. 2) for a distance of about 10 mm. to the striated muscle fibers of the levator (*B*, Fig. 2), where the smooth and striated fibers interlace (*2*, Fig. 4).

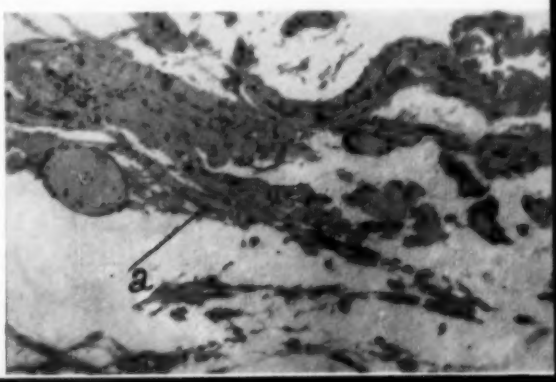
Below Müller's muscle is the conjunctiva of the upper fornix (*8*, Fig. 2); above is the aponeurosis, identified histologically as moderately dense connective tissue (Figs. 1 to 3). Because the aponeurosis and Müller's muscle are so intimately attached, these two layers are always reflected together in operations for resection of the levator (Berke [14]). It is to be noted that the combined thickness of these layers is less than that of the cornea (Fig. 2). Because of this delicate structure, these layers are easily torn and are sometimes difficult to identify in operations on the levator.

Near the upper border of the tarsus the aponeurosis blends with the septum orbitale to form a barrier to prolapse of orbital fat into the tissues of the upper lid (Fig. 2).‖ Beyond the upper edge of the tarsus the aponeurosis divides into fine fibers, which insert into the anterior surface of the tarsus, the overlying orbicularis muscle, and the adjacent skin to produce the upper lid fold, as illustrated to the right of *A* in Figure 2.

It is therefore obvious that the skin, the orbicularis, and the lashes are supported mainly by the aponeurosis, while the tarsus is pulled upward chiefly by Müller's muscle.

Fig. 6.—High-power magnification of area *A* indicated in Figure 5, showing large bundles of smooth muscle fibers (*a*) present in anterior portion of muscle.

Fig. 7.—High-power magnification of area *B* as indicated in Figure 5, showing normal striated muscle fibers (*a*) from levator muscle.



‖ The forward displacement of the septum orbitale in Figures 1 and 2 gives an erroneous impression of the normal relationship of these structures.

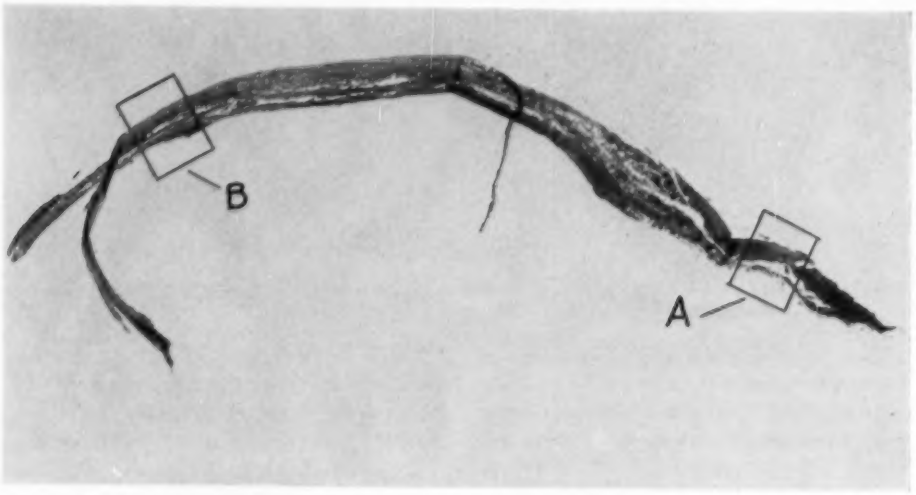


Fig. 8.—Low-power magnification of sagittal section taken from an excised levator in a case of ptosis following birth trauma (Table 3).

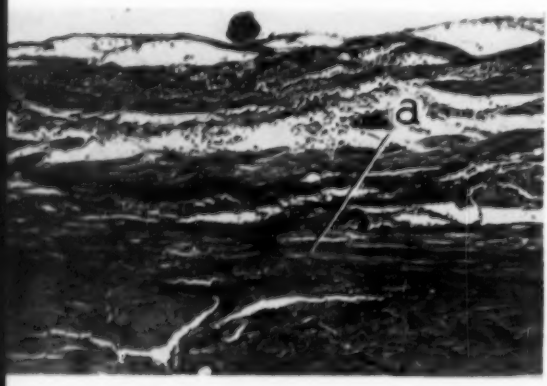
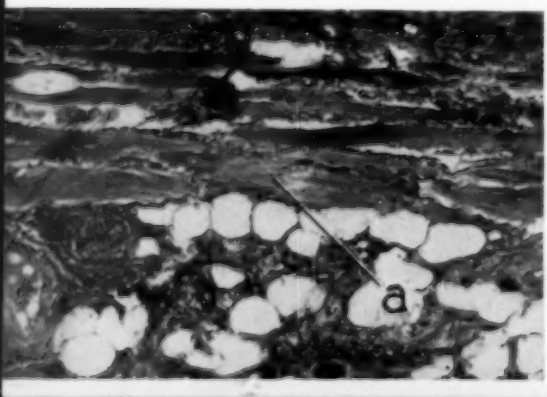


Fig. 9.—High magnification of area *A* as indicated in Figure 8, showing large bundles of smooth muscle fibers at *a*.

Fig. 10.—High magnification of area *B* as indicated in Figure 8, showing normal striated muscle fibers at *a*.



HISTOLOGICAL FINDINGS OF LEVATOR MUSCLE IN PTOSIS

The histological material for this study is made up of 116 biopsy specimens of the anterior part of the levator, excised from patients with assorted types of ptosis. Four of these specimens came from patients with the jaw-winking phenomenon in whom the superior rectus muscle was utilized to correct the ptosis; the rest came from modified Blaskovics operations for resection of the levator (Berke[15]). Of this number, 34 had to be discarded for various reasons, leaving 82 specimens for histological examination.¶

Each specimen, varying from 12 to 30 mm. in length, was sectioned lengthwise so as to give a sample from each third of the specimen. The trichrome stain was used because it stains the smooth and striated muscle fibers pink and the connective tissue blue. In each

¶ The causes for elimination were as follows: Seventeen cases were discarded because a previous ptosis operation had distorted the anatomy; 8 cases, because the specimen was bunched or sectioned wrong; 5 cases, because the specimen was too short, and 4 cases, because the history was incomplete.

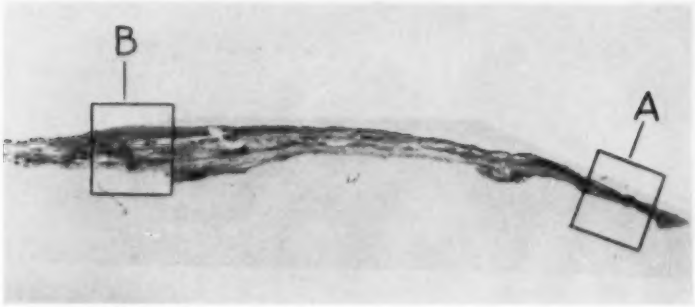


Fig. 11.—Low-power magnification of sagittal section in case of ptosis associated with jaw-winking phenomenon of Marcus Gunn (Table 1).

TABLE 1.—*Summary of Histological Findings in Eighty-Two Assorted Cases of Ptosis*

Type of Ptosis	No. of Cases	Amount of Ptosis, Mm.	Cases with Skeletal Muscle Fibers from Levator, %
Acquired ptosis	8	2.8	100
Congenital ptosis associated with birth trauma	5	3.6	100
Congenital ptosis associated with jaw winking	5	3.5	100
Congenital ptosis of 2 mm.	5	2	100
Congenital ptosis of 3 mm.	22	3	54
Congenital ptosis of 4 mm. or more	37	4.8	0
Total no. of cases	82	...	...

specimen a special search was made for striated muscle fibers of the levator.#

In every specimen smooth muscle fibers (Müller's muscle) were found, which sometimes joined great numbers of normal-appearing levator striated muscle fibers. In other specimens striated fibers were absent and the smooth muscle fibers ended in loose areolar tissue rather than in abundant striated muscle fibers. On the basis of these findings, the history of the case, and the clinical examination, we were able to divide our assorted cases into six groups (Table 1).

1. *Acquired Ptosis.*—Eight biopsy specimens in cases of acquired ptosis were available for study. In each, an abundance of

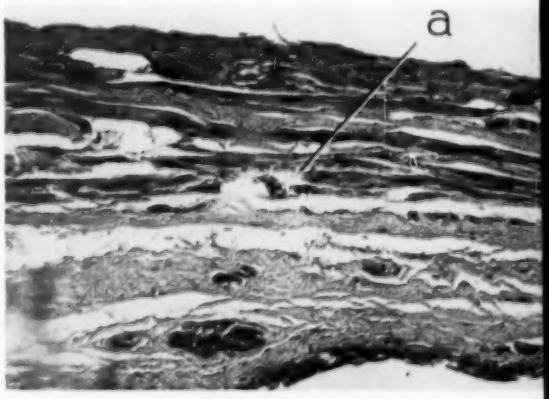
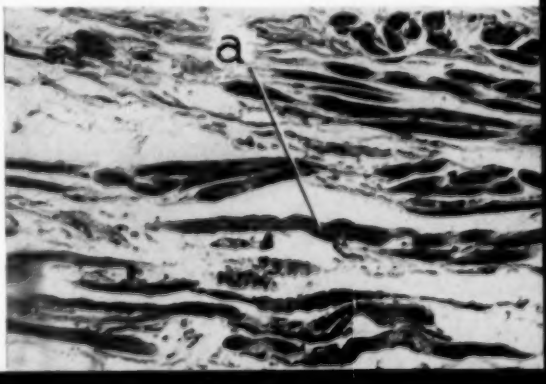


Fig. 12.—High magnification of area *A* as indicated in Figure 11, showing parallel bundles of smooth muscle fibers (*a*) located in anterior portion of levator.

Fig. 13.—High magnification of area *B* as indicated in Figure 11, showing normal striated muscle fibers (*a*) from levator muscle.



Where a Motais type of operation had been done before, transplanted fibers of the superior rectus muscle could be mistaken for striated muscle fibers from the levator. Also, where a previous resection of the levator had been done, bundles of the orbicularis muscle were often found in the biopsy tissue. To avoid confusion, all cases in which such operations had been performed were discarded. In other cases, in which there was any question as to the nature of the tissues concerned, the specimens were seen in consultation with Dr. Arthur Purdy Stout, Pathologist, Presbyterian Hospital, New York.

Fig. 14.—Low-power magnification of sagittal section taken from excised levator in a case of ptosis of no more than 2 mm. (Table 4).

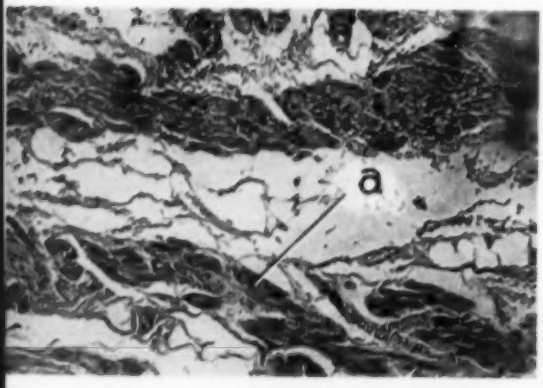
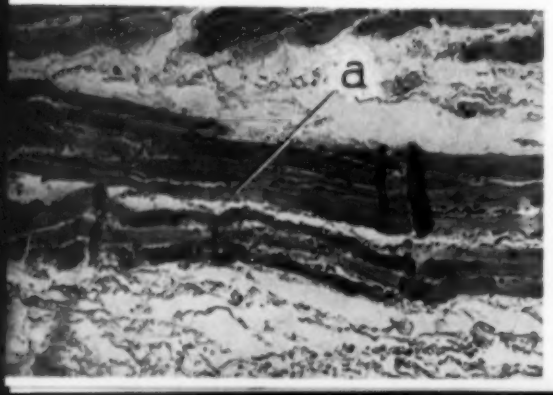


Fig. 15.—High magnification of area *A* indicated in Figure 14, showing large bundles of smooth muscle fibers (*a*) at anterior end of levator muscle.

normal-appearing levator striated muscle fibers were found. Figures 5, 6, and 7 illustrate the histological findings. In only one of these did the levator appear abnormal histologically. In this case lymphocytic infiltration of the striated muscle fibers of a nonspecific nature was noted.*

* Opinion of Dr. Arthur P. Stout.

Fig. 16.—High magnification of area *B* as indicated in Figure 11, showing normal striated muscle fibers (*a*) of levator.



From this study we may conclude that levator striated muscle fibers are always present in acquired ptosis provided sufficient levator tissue is excised.†

2. Congenital Ptosis Associated with Birth Trauma.—In five cases with a definite history of birth trauma and clinical evidence of a more or less complete external third nerve paralysis, many normal-appearing striated muscle fibers of the levator were present, as illustrated in Figures 8, 9, and 10. Therefore, we conclude that striated muscle fibers of the levator are always present in ptosis secondary to birth trauma.

3. Congenital Ptosis Associated with Jaw-Winking Phenomenon of Marcus Gunn.—In each of the five cases of this type an abundance of normal-appearing striated levator fibers were present. From this we conclude that striated muscle fibers of the levator are always present in the Marcus Gunn syndrome (Figs. 11, 12, and 13).

4. Congenital Ptosis of 2 Mm.—In the five cases in this category some normal-appearing striated muscle fibers were found (Figs. 14, 15, and 16). In all, however, the fibers seemed fewer in number and sparser than in the groups already discussed. Therefore, we believe that a few striated muscle

† Five other cases of acquired ptosis had to be eliminated: two because the specimen was too short and three because the levator had receded too deep into the depths of the orbit to be reached. In each of the latter, the levator had accidentally been severed above the tarsus during previous operations on the upper lid.

Fig. 17.—Low-power magnification of a sagittal section of levator muscle excised in a case of ptosis of 3 mm. (Table 5).

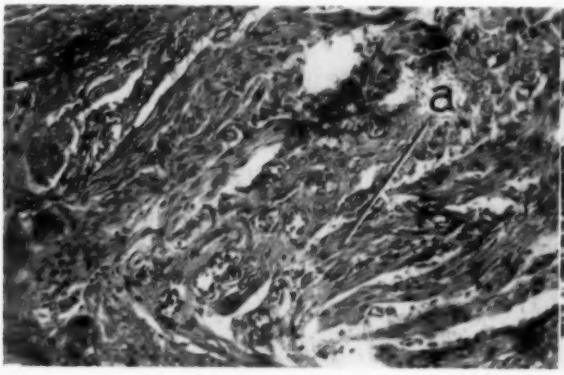


Fig. 18.—High magnification of area *A* as indicated in Figure 17, showing the large bundles of smooth muscle fibers (*a*) present in anterior portion of muscle.

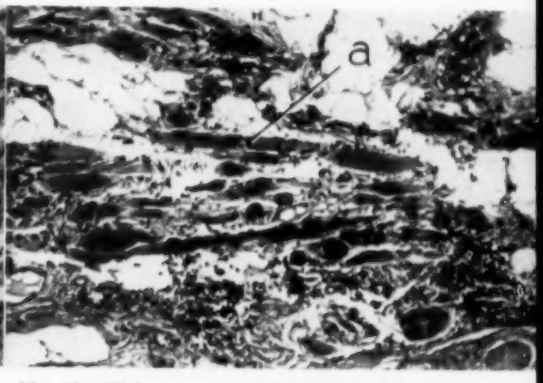
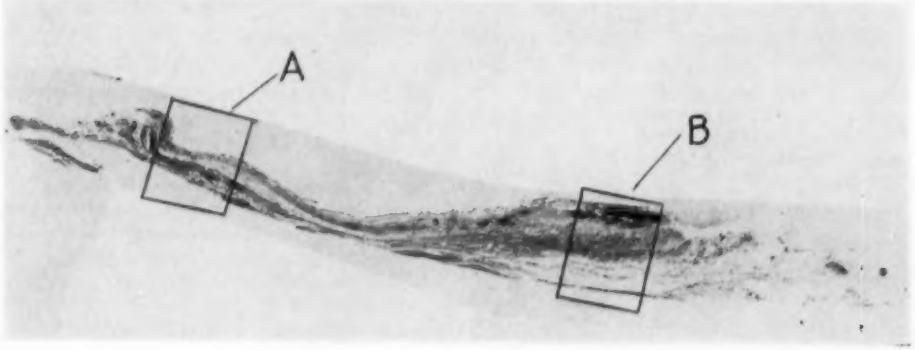


Fig. 19.—High-power magnification of area *B* as indicated in Figure 17, showing normal striated muscle fibers (*a*) surrounded by loose areolar tissue.

fibers will always be present in cases of congenital ptosis of 2 mm. or less.

5. *Congenital Ptosis of 3 Mm.*—In 22 congenital cases the ptosis measured 3 mm. in the primary position. Twelve (54%) of these showed sparse, normal-appearing striated muscle fibers where an abundance of these fibers would normally be found (Figs. 17, 18, and 19). In the other 10 cases striated

Fig. 20.—Low-power view of sagittal section excised from levator muscle in a case of ptosis of 3 mm. (Table 6).



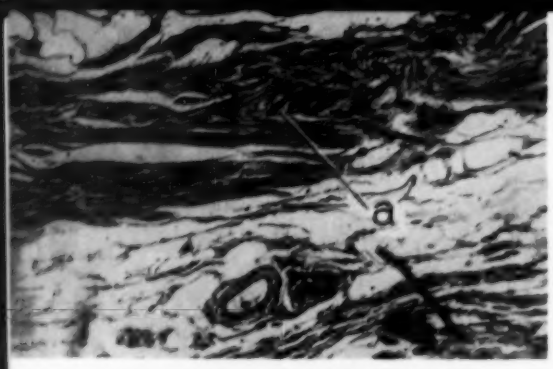
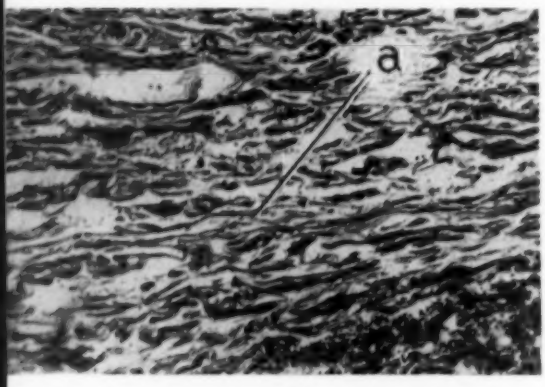


Fig. 21.—High magnification of area *A* as indicated in Figure 20, showing normal smooth muscle fibers (*a*) in anterior portion of levator muscle.

Fig. 22.—High magnification of area *B* as indicated in Figure 20, showing absence of striated muscle fibers (*a*) and presence only of loose areolar tissue.



muscle fibers were completely absent, but Müller's muscle was always present and seemed to end in loose areolar tissue, in place of striated muscle fibers (Figs. 20, 21, and 22).

From this study we conclude that the striated muscle fibers of the levator are sparse or entirely absent in congenital cases of ptosis of 3 mm.

6. Congenital Ptosis of 4 Mm. or More.—There were 37 cases of congenital ptosis in which the drooping measured more than 4 mm. Most of these cases showed poor levator action. Nevertheless, resection of the levator was done to test Blaskovics'[16] contention that the results of this operation are uniformly satisfactory, even when the levator is paralyzed or absent.

As indicated in Table 1, none of these 37 cases showed levator striated muscle fibers, even though as much as 30 mm. of stretched-out levator tissue was excised. In these cases Müller's muscle was always present but ended in loose areolar tissue in place of striated muscle fibers (Figs. 23, 24, and 25).

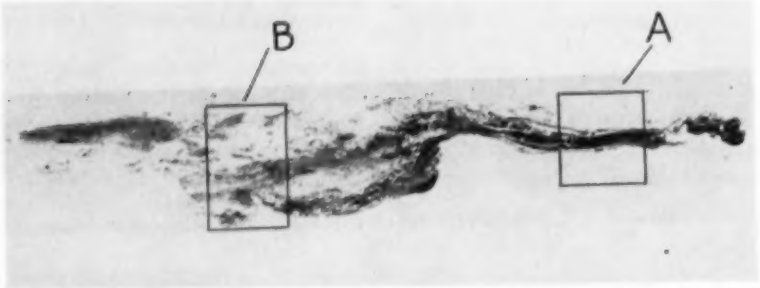


Fig. 23.—Low-power magnification of sagittal section of levator muscle excised in a case of ptosis of 4 mm.

Fig. 24.—High magnification of area *A* as designated in Figure 23, showing normal smooth muscle fibers (*a*) in anterior portion of levator muscle.

From these data we conclude that levator striated muscle fibers are always absent in congenital ptosis of 4 mm. or more.‡

‡ The absence of striated muscle fibers in the anterior part of the levator does not preclude the possibility of their presence farther back in the muscle. As a matter of fact, scattered striated fibers probably would be found in most cases of congenital ptosis if the entire levator could be examined histologically.

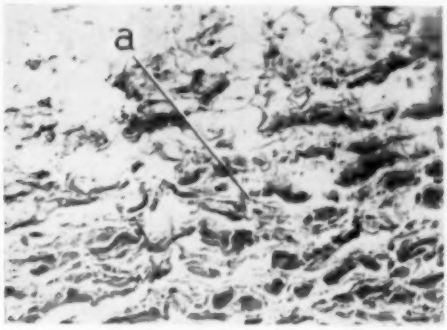


Fig. 25.—High magnification of area *B* as designated in Figure 23, showing absence of striated muscle fibers (*a*) but presence of loose areolar tissue.

of ptosis present in each of eight cases of acquired ptosis before and after operation, the cause of the ptosis in each case, and the reason for undercorrection. It should be noted that the average ptosis was relatively great (4.2 mm.) before operation, the average residual ptosis was 1.5 mm., and the average amount of correction was 2.7 mm. In only one case did the operation result in complete failure, and that was attributed to pulling out of the sutures secondary to severe postoperative edema. In the rest of the cases undercorrection occurred mainly because of insufficient resection. Of the entire group, 35.7% had a good or excellent result from the operation.§

TABLE 2.—*Acquired Ptosis*

Case	Millimeters of Ptosis: Before	After	Improvement	Cause of Ptosis	Cause of Undercorrection
1	8	2	6	Developed spontaneously at age 21	Insufficient resection
2	3	0	3	Head injury in football game	Excellent result
3	3	2	1	Severe keratitis and conjunctivitis	Insufficient resection
4	2	0	2	Horner's syndrome from hygroma of neck	Excellent result
5	4	0	4	Fibroma of right frontal bone	Excellent result
6	4	2	2	Thyroid dysfunction	Insufficient resection
7	6	2	4	Thyroid dysfunction	Insufficient resection
8	4	4	0	Developed spontaneously at age 4½ yr.	Sutures pulled out
Av.	4.2	1.5	2.7	37.5% excellent results	

EFFECT OF SKELETAL MUSCLE FIBERS ON FINAL RESULT OF RESECTION OF LEVATOR

In a recent survey of 91 operations for shortening the levator muscle (Berke [15]), we concluded that when undercorrection occurred in the presence of good levator action, the chief cause for failure was insufficient resection, but that when the levator action was poor, the main cause for failure was inadequate levator tissue. In that survey no attempt was made to ascertain what effect the presence or absence of striated muscle fibers had on the operative result. In order to answer this question, our cases were divided into groups (Table 1), and the percentage of satisfactory corrections attained for each group was correlated with the amount of levator striated muscle fibers present.

1. *Results of Resection of Levator in Acquired Ptosis.*—Table 2 shows the amount

From this study it would seem that in all cases of acquired ptosis an excellent result should follow resection of the levator if sufficient levator tissue is excised and care taken to prevent pulling out of the sutures (Fig. 26).

However, it should be pointed out that the causes of acquired ptosis are so varied that one cannot safely generalize. Each case must be treated individually. For example, more levator tissue should be removed when the levator is very weak than when a normal muscle has been merely severed. Therefore, the result of resection of the levator in acquired ptosis may depend more on the cause of the ptosis than on the presence of striated muscle fibers.

§ By "good" we mean 1 mm. of undercorrection; by "excellent," no residual ptosis.

Fig. 26.—Ptosis of right eye, which developed spontaneously at age of 21 years. No history of injury. *A*, before operation; *B*, after resection of levator of right eye.

2. Results of Resection of Levator in Congenital Ptosis Associated with Birth Trauma.—In five cases the ptosis was associated with a history of birth trauma and clinical evidence of a partial third nerve paresis.

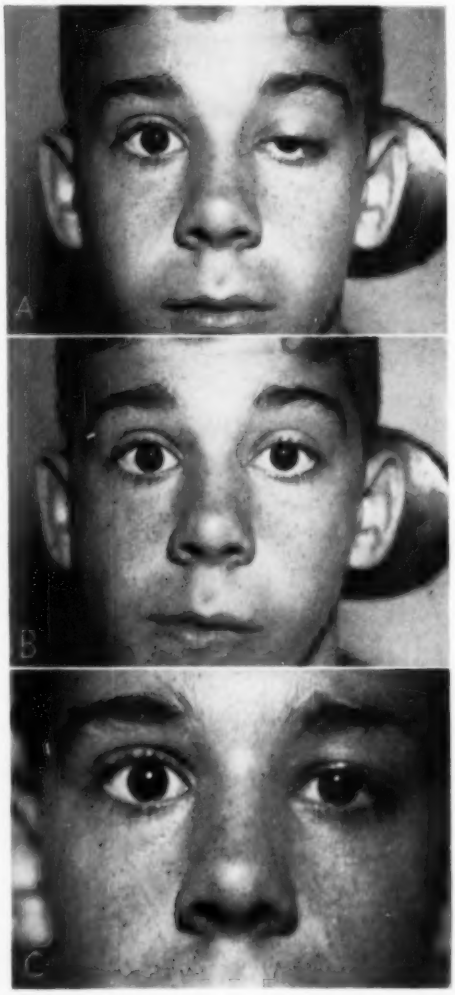
TABLE 3.—*Congenital Ptosis Associated with Birth Trauma*
(Third Nerve Paresis)

	Millimeters of Ptosis			
Case	Before	After	Improvement	Cause of Undercorrection
1	6	2	4	Insufficient levator resection
2	3	2	1	Insufficient levator resection
3	3	0	3	Excellent result in primary position
4	5	4	1	Sutures pulled out second postoperative day
5	3	2	1	Insufficient levator resection
Average	4	2	2	20% excellent results

Table 3 indicates the amount of ptosis present before and after operation, together with a list of the causes for undercorrection. The average amount of preoperative ptosis for this group was 4 mm. and the average residual ptosis 2 mm. The chief cause for undercorrection was attributed to insufficient resection or to stretching of the levator muscle, only two of the five cases getting more than 1 mm. of improvement from the operation.‖

‖ The poor results from operation in this group could be attributed perhaps to the lack of nerve impulses, because shortening a paralyzed muscle does not produce a permanent correction, owing to the tendency of the paralyzed muscle to stretch with time.

Fig. 27.—Case of jaw-winking phenomenon of Marcus Gunn involving left eye. A resection of the levator was performed utilizing a portion of the superior rectus to elevate the lid. *A*, before operation; *B*, jaw-winking phenomenon with chin deviated to right; *C*, postoperative result.



These results would tend to show that the presence of levator striated muscle fibers in this group did not of itself assure complete correction of the ptosis. Perhaps removal of more levator tissue at the time of operation might have produced better results. Or perhaps cases of third nerve paralysis, especially cases associated with paralysis of the superior rectus muscle, are doomed to failure because of the corneal exposure and blepharospasm which usually occur in these cases.

3. Results of Resection of Levator in Congenital Ptosis Associated with Jaw-Winking Phenomenon of Marcus Gunn.—There were five cases of this type in which a biopsy specimen of the levator was taken. In only one case was the levator resected, the remainder having a modified Motais procedure to correct the ptosis. In this case the operation resulted in failure because of a combination of things: insufficient resection, stretching of the levator muscle, and pulling out of the sutures. From this one case it would seem that even though striated muscle fibers are present, resection of the levator in patients with jaw winking is ill-advised (Fig. 27).

TABLE 4.—*Congenital Ptosis of 2 Mm.*
(With Skeletal Muscle Fibers from Levator Muscle)

Case	Millimeters of Ptosis: Before	After	Improvement	Cause of Undercorrection
1	2	1	1	Insufficient resection
2	2	0	2	Excellent result
3	2	0	2	Excellent result
4	2	0	2	Excellent result
5	2	0	2	Excellent result
Average	2	2	1.8	100% good or excellent results

4. Results of Resection of Levator in Congenital Ptosis of 2 Mm.—Table 4 lists the amount of ptosis before and after operation in five cases of 2 mm. of ptosis, in each of which striated muscle fibers from the levator were found, although not in the abundance characteristic of acquired ptosis. In all except one case the ptosis was fully corrected by resection of the levator muscle (Fig. 28).

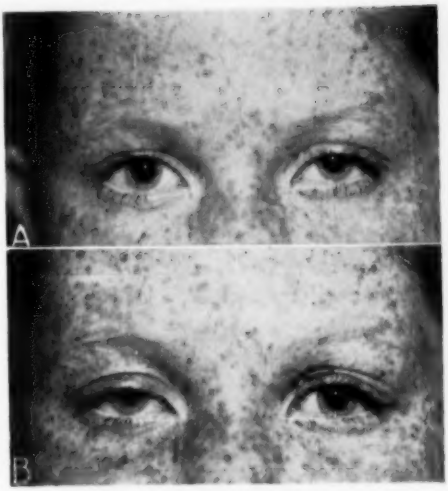


Fig. 28.—Congenital ptosis of 2 mm. Resection of the levator of left eye was carried out, with satisfactory result. *A*, before operation; *B*, after operation.

These figures would tend to indicate that resection of the levator in congenital ptosis of 2 mm. should always give an excellent or good result if sufficient levator tissue is resected and the sutures do not pull out.

5. Results of Resection of Levator in Congenital Ptosis of 3 Mm. in Which Levator Skeletal Muscle Fibers Were Present.—In 12 cases of congenital ptosis of 3 mm. striated muscle fibers were found (Table 5). In

TABLE 5.—*Congenital Ptosis of 3 Mm.*
(With Skeletal Muscle Fibers from Levator Muscle)

Case	Millimeters of Ptosis: Before	After	Improvement	Cause of Undercorrection
1	3	3	0	Pulling out of sutures
2	3	0	3	Excellent result
3	3	1	2	Sutures pulled out
4	3	1	2	Sutures pulled out
5	3	0	3	Excellent result
6	3	0	3	Excellent result
7	3	3	0	Levator stretched or sutures failed
8	3	0	3	Excellent result
9	3	0	3	Excellent result
10	3	2	1	Insufficient resection
11	3	1	2	Insufficient resection
12	3	0	3	Excellent result
Average	3	0.9	2.1	75% good or excellent results

all of these the muscle fibers were spread apart by orbital fat or loose areolar tissue, being very sparse as compared with the number of fibers seen in patients of 2 mm. of ptosis.¶

Nine, or 75%, of this group derived a good or excellent result from the operation, the average amount of residual ptosis being only 0.9 mm. Undercorrection was attributed to insufficient levator resection or to pulling out of the sutures.

When the results of operation and the number of levator muscle fibers of this group are compared with those for the patients with 2 mm. of ptosis, one gets the impression that the number of striated muscle fibers present in congenital ptosis determines the amount of preoperative ptosis, as well as the percentage of satisfactory postoperative results, and that undercorrection, when it occurs, is due either to insufficient resection or to pulling out of the sutures.

TABLE 6.—*Congenital Ptosis of 3 Mm.*
(Without Skeletal Muscle Fibers from the Levator)

Case	Millimeters of Ptosis: Before	After	Improvement	Cause of Undercorrection
1	3	1	2	Insufficient resection
2	3	0	3	Excellent result
3	3	0	3	Excellent result
4	3	2	1	Sutures pulled out
5	3	0	3	Excellent result
6	3	0	3	Excellent result
7	3	1	2	Extraocular muscle imbalance
8	3	4	1	Sutures failed
9	3	0	3	Excellent result
10	3	2	1	Insufficient levator resection
Average	3	1	2	70% good or excellent results

6. Results in Congenital Ptosis of 3 Mm. in Which Levator Skeletal Muscle Fibers Were Absent.—In 10 cases of congenital ptosis of 3 mm., no levator striated muscle fibers were found, even though each specimen was sufficiently long to include them had they been present.

Seventy per cent of this group (Table 6) got a good or excellent result from the operation, with an average residual ptosis of 1 mm. These results compare very favorably with the preceding group, in which the average preoperative ptosis also measured 3 mm. but in which a few scattered striated muscle fibers were present.

From these data it would seem that the percentage of good results in patients with 3 mm. of ptosis does not depend entirely on finding striated muscle fibers in the biopsy specimen. However, as already mentioned, we believe that such fibers must exist farther back in the levator muscle; otherwise, the similarity of the results in the two groups would be difficult to explain.

Tables 5 and 6 also serve to emphasize the importance of other factors, such as insufficient resection and pulling out of the sutures, in determining the percentage of good results from resection of the levator in congenital ptosis.

7. Results in Congenital Ptosis of 4 Mm. or More.—In Table 7 are listed 37 cases of congenital ptosis, varying from 4 to 8 mm. in amount, in none of which levator striated muscle fibers were found. The ptosis averaged 4.9 mm. before and 2.3 mm. after operation, with only 35% of the group getting a good or excellent result. The main cause for undercorrection here was poorly developed levator tissue associated with poor levator action.

From these figures one may conclude that the percentage of good or excellent results following resection of the levator decreases considerably when the amount of ptosis is more than 3 mm.

Because of the poor results in this group, we must conclude that undercorrection following resection of the levator is the rule when the levator action is poor or when the ptosis measures more than 3 mm. (Fig. 29). This conclusion would tend to vitiate Blaskovics' contention that his operation gives

¶ It is well known that the histological appearance of striated muscle varies with the state of contraction and the amount of handling. Nevertheless, these fibers appeared normal except that crossed striations were seldom seen.

TABLE 7.—*Congenital Ptosis of 4 Mm. or More* (Without Skeletal Muscle Fibers from Levator)

Case	Millimeters of Ptosis: Before	After	Improvement	Cause of Undercorrection
1	8	8	0	Inadequate levator tissue
2	8	8	0	Inadequate levator tissue
3	7	2	5	Inadequate levator tissue
4	6	2	4	Poorly developed levator
5	6	5	1	Inadequate levator tissue
6	6	3	3	Inadequate levator tissue
7	6	0	6	Excellent result
8	5	0	5	Excellent result
9	5	2	3	Poor levator tissue
10	5	3	2	Insufficient levator resection
11	5	4	1	Insufficient levator resection
12	5	5	0	Inadequate levator tissue
13	5	5	0	Poor levator tissue
14	5	3	2	Poor levator tissue
15	5	0	5	Excellent result
16	5	3	2	Sutures pulled out
17	5	3	2	Insufficient resection
18	5	1	4	Bilateral ptosis
19	5	0	5	Excellent result
20	5	2	3	Inadequate levator tissue
21	5	3	2	Inadequate levator tissue
22	5	3	2	Edema—5-day follow-up only
23	4	4	0	Inadequate levator tissue
24	4	1	3	Excellent result until hit in eye with ball
25	4	2	2	Bilateral ptosis
26	4	1	3	Insufficient levator resection
27	4	2	2	Bilateral ptosis
28	4	3	1	Inadequate levator tissue
29	4	0	4	Excellent result
30	4	2	2	Bilateral ptosis
31	4	3	1	Inadequate levator tissue
32	4	1	3	Levator very thin
33	4	0	4	Excellent result
34	4	0	4	Excellent result
35	4	2	2	Bilateral ptosis
36	4	0	4	Adhesion to superior oblique caused overcorrection
37	4	0	4	Excellent result
Average	4.9	2.3	2.59	35% good or excellent results

good results "even in those cases in which this muscle is completely paralyzed or atrophic" (de Blaskovics [16]).

ETIOLOGY OF CONGENITAL PTOSIS

After eliminating congenital ptosis caused by birth trauma and ptosis associated with the jaw-winking phenomenon, in both of which there is an abundance of levator striated muscle fibers, we have an intriguing group of 64 cases in which the cause of the ptosis is still controversial, some investigators (Siemerling,[4] Wilbrand and Saenger,[5] Spaeth [17]) contending that the cause is primarily a lesion of the nervous system, and others that it is a failure of muscular development.

From this study and a review of the scanty literature, we believe that congenital ptosis is a developmental anomaly of the levator muscle, for the following reasons: First, all

Fig. 29.—Case of ptosis of the left eye of greater than 4 mm. A resection of the levator was performed, giving definite improvement, with good lid fold. (A previous ptosis operation, of unknown type, had been done elsewhere, leaving a scar in the left upper lid.) *A*, before operation; *B*, after operation.

available anatomical or histological studies to date have shown a decrease or a complete absence of the muscle fibers of the levator in congenital ptosis. Second, case reports of ptosis associated with faulty insertion, bifurcation of the muscles, or incomplete separation of the superior rectus and levator muscles can be more easily explained on the basis of faulty muscular development than by postulating a lesion of the central nervous system. Third, the pupillary and accommodation reflexes are scarcely ever involved in

congenital ptosis.# One would certainly expect such involvement if ptosis were caused by a lesion of the third nerve or of its nucleus. Fourth, because the levator develops from the superior rectus muscle comparatively late in embryonic life (Mann[19]), and because it is the most recently acquired of the extraocular muscles phylogenetically (Neal,[20] Groyer*), it is more vulnerable to abnormal development. Fifth, since the extraocular muscles develop independently of their nerve supply, one should always find skeletal muscle fibers in congenital ptosis if the primary cause of the ptosis were a lesion of the central nervous system.

SUMMARY AND COMMENT

Histology of Levator Muscle in Ptosis.—To augment the meager knowledge of the levator muscle in acquired and congenital ptosis, 84 biopsy specimens were studied.

These specimens were long enough to include all of Müller's muscle and some of the striated muscle fibers of the levator, so that, had striated muscle fibers been present, they would have been noted in the biopsy specimen. We realize, of course, that these specimens cannot possibly represent the histological condition of the entire levator muscle. Nevertheless, this study revealed some very interesting and significant facts. For example, abundant normal-appearing striated muscle fibers were always found in acquired ptosis, in congenital third nerve paralysis, and in patients with the jaw-winking phenomenon of Marcus Gunn. However, in congenital ptosis, striated muscle fibers were always sparse or absent, so that if the ptosis measured only 2 mm., a few striated muscle fibers were always present; if 4 mm. or more, these fibers were always present, but if exactly 3 mm., about half of the cases showed such fibers and half did not.

The absence of striated muscle fibers in all cases of congenital ptosis of more than 3 mm. and their presence in all cases of less than this amount would tend to indicate that the amount of ptosis in a given case depends on the number of striated muscle fibers present.

Effect of Levator Structure on Results of Levator Resection.—Most ophthalmologists believe that resection of the levator for ptosis is not indicated when the function of this muscle is greatly reduced or absent, the inference being that the muscle is too frail or delicate to support the upper lid. However, Blaskovics[16] stated that his operation is successful "even when the muscle is absent."†

With Blaskovics' statement in mind, and the knowledge that resection of the levator is less successful when the levator function is poor, we were anxious to learn whether the histological nature of this muscle was an important factor in the success of the operation. For this purpose, we divided our cases in seven groups in order to compare the results for each group.

In acquired ptosis, in which the levator muscle appeared normal histologically, the percentage of good or excellent results was only fair (37.5%) for the group as a whole, the chief cause for failure being insufficient resection. This study would tend to indicate that satisfactory results in acquired ptosis must depend on factors other than the mere presence of striated muscle fibers.

The percentage of good results in congenital ptosis associated with a third nerve paresis was only 20% for the group as a whole, the chief cause for failure being insufficient resection and pulling out of the sutures, the effect being augmented by corneal irritation and blepharospasm, especially when the superior rectus was very weak. Because there were only five cases of this type, we hesitate to draw any final conclusions except to state that the presence of normal-appearing striated muscle fibers in these cases did not of itself assure a high percentage of good or excellent results.

Rodin and Barkan[15] were able to find only one undisputed case of hereditary congenital total ophthalmoplegia in the literature.

* References 21 through 23.

† Blaskovics must have meant "even when the muscle function is absent," for, obviously, it is impossible to resect something that does not exist.

Resection of the levator was done in one case of the jaw-winking phenomenon, with complete failure. Because of this and other considerations, we do not believe this operation is indicated for ptosis of this type.

The best results (100% good or excellent) were obtained in a group of cases of congenital ptosis of 2 mm., in all of which some fibers from the levator muscle were found (Table 8). The poorest results (35% good or excellent) in congenital ptosis occurred in patients with more than 3 mm. of ptosis, in none of whom were striated muscle fibers found. When the congenital ptosis measured exactly 3 mm., the good or excellent results varied from 70% to 75%, depending on the absence or presence of striated muscle fibers. From this study we conclude that the results of this operation in congenital ptosis depend on the presence of levator striated muscle fibers—the greater the number of fibers present, the better the results; the fewer the fibers, the poorer the results.

TABLE 8.—*Comparison of the Results of Resection of the Levator in Sixty-Four Cases of Congenital Ptosis*

Type of Congenital Ptosis	No. of Cases	Average Amount of Ptosis, Mm.		Percentage of Good or Excellent Results
		Before Operation	After Operation	After Operation
With skeletal muscle fibers	5	2.0	0.2	100
With skeletal muscle fibers	12	3.0	0.9	75
Without skeletal muscle fibers	10	3.0	1.0	70
Without skeletal muscle fibers	37	4.9	2.3	35
Total number of cases	64			

Etiology of Congenital Ptosis.—These histological studies tend to confirm the theory that congenital ptosis, when not associated with birth trauma or jaw winking, is primarily the result of defective muscular development.

CONCLUSIONS

A. A histological study of 82 biopsy specimens from resection of the levator established the following findings:

1. Müller's upper lid muscle is always present in acquired and congenital ptosis.

2. Striated muscle fibers of the levator are always found in acquired ptosis, in ptosis due to birth trauma, and in ptosis associated with the jaw-winking phenomenon of Marcus Gunn.

3. Striated muscle fibers of the levator are always found in congenital ptosis of 2 mm. or less.

4. Levator striated muscle fibers are present in only 54% of cases of congenital ptosis of 3 mm.

5. Levator striated muscle fibers are never found in congenital ptosis of 4 mm. or more.

B. The results of resection of the levator for each type of ptosis would indicate the following:

1. The presence of numerous striated muscle fibers in acquired ptosis, in ptosis from birth trauma, or in ptosis associated with the jaw-winking phenomenon does not of itself assure a high percentage of satisfactory postoperative results.

2. The number of striated fibers present in congenital ptosis seems to be an important factor in determining the final result, because the highest percentage of satisfactory results occurred when these fibers were present and the lowest percentage when they were absent.

C. These studies on the histology of the levator muscle would favor the theory that congenital ptosis, not associated with birth trauma or the jaw-winking phenomenon, is primarily a defective structural development of the levator muscle.

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Fundus Photography in Color with Zirconium Arc Lamp as Light Source

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In the course of a study of retinal atrophy in dogs, it became necessary to obtain colored photographs of the fundus. A Bausch & Lomb fundus camera was used for this purpose, with a carbon arc as its light source.

The disadvantages of the carbon arc in human fundus photography are numerous and are too familiar to ophthalmologists to require enumeration here (Hansell and Beeson,[1] 1953). An additional difficulty arises during protracted observations on experimental animals, when the lids are held open by a speculum or by sutures. Under these conditions, with the lids immobilized, the cornea tends to dry out; this tendency is greatly increased by the heat from the carbon arc. To obviate desiccation of the cornea, the eye must either be irrigated with saline at frequent intervals (our method) or have a special contact lens fitted to it (method of Clasen and associates[2]).

Animals cannot, of course, be asked to fix their gaze on a fixation light, and must be placed under a general anesthetic prior to fundus photography. All the required table and camera movements necessary to locate the field and bring it into focus take considerably longer than with a human subject. Thus, the arc lamp necessarily burns for a longer period in obtaining any given number of photographs. As a result of this prolonged operation, we found that products of carbon pencil combustion became deposited on the face of the condenser lens. In addition, on the two cameras tested by us, the heat of this prolonged operation sometimes resulted in arrest of the clockwork mechanism which advances the carbon pencils. Thus, the arc would go out just as the operator was ready to press the cable release. On numerous other occasions the light was found to flicker because the carbons were not being advanced at a uniform rate once the clockwork became hot. This resulted in momentary changes in the light intensity, and consequently in its color temperature, which made correct exposure and faithful color rendition difficult.

Although there are doors in the lamp house which give access to both the horizontal and the vertical carbon, the latter door cannot be opened without demounting the lamp house. Thus, when the carbon burned out during a photographic session, it was necessary to wear asbestos gloves in handling the extremely hot lamp house and in readjusting the centering setscrews. The latter operation was necessary every time the carbons were changed. After operating two of the cameras for several months, we became increasingly interested in finding a substitute for the carbon arc as a source of light.

Several light sources were tested, and a 100-watt zirconium concentrated arc lamp was found to be satisfactory.[3] The model selected was the Sylvania C100/P, in which the end of the lamp is a polished optical flat (Fig. 1). The lamp and its power supply unit were purchased commercially. A simple housing was made for the lamp from copper tubing and attached to the camera by means of the same adapter ring used for the carbon arc lamp house (Fig. 3).

The zirconium arc lamp burns at about 400 F and has a life of about 1000 hours. The long life is a great advantage, since once the lamp is centered it does not require readjustment at every photographic session. The lamp is filled with argon, and it produces a steady,

From the Brookhaven National Laboratory.

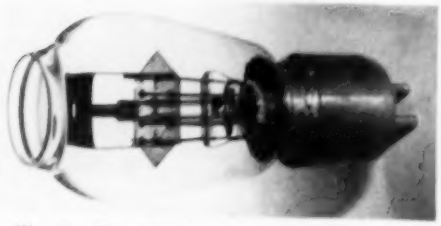
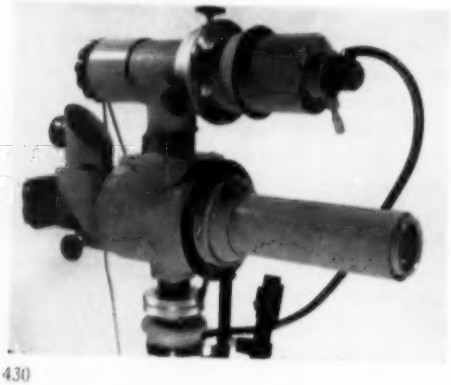


Fig. 1.—The zirconium arc lamp shown in the horizontal position in which it is used in the fundus camera. The glass at the left end is a polished optical flat.

flickerless light, resembling a filament lamp rather than an arc lamp in this respect. Although the intensity of the 100-watt lamp is less than that of the carbon arc which it replaced, we found that it gave slightly more effective illumination on the fundus than the old light source. The light-emitting area itself was smaller than that of the carbon arc. The effect of this smaller light source was to improve the modeling of the blood vessels in the photographs, giving them a three-dimensional effect rather than a flat one. An additional advantage is the fact that the zirconium arc lamp maintains a uniform brightness over a wide variation of lamp input voltage. This characteristic is particularly important when using color films, all of which are extremely sensitive to even slight changes in the color temperature of the light source.

In the original equipment, a yellow color-correcting glass filter was used to balance the carbon arc flame for Kodachrome daylight film. In addition, a glass heat-absorbing filter was interposed between the prism and the remainder of the optical system. We removed the yellow filter and changed to Kodachrome type A film, which is balanced for light of 3400° K. The zirconium arc light has a color temperature of 3200° K; the 200-degree difference was largely corrected by the bluish glass in the heat-absorbing filter, which was left in place for this purpose.

Fig. 2.—The lamp and its housing in position on the fundus camera. The current supply is through a four-conductor cable and a standard four-pin radio tube socket. The tapered sleeve on the lamp house traps light escaping through the ventilating slots but permits air circulation.



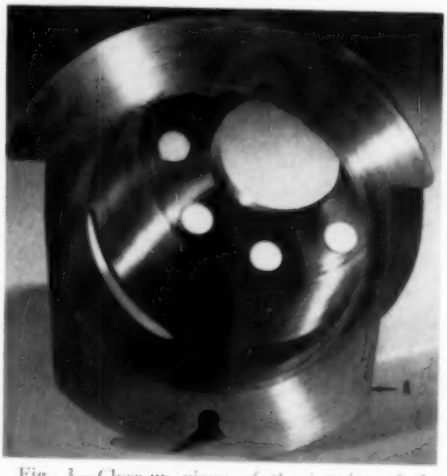


Fig. 3.—Close-up views of the interior of the lamp house. There are four slots and eight circular holes for ventilation. The adapter ring (*A*) was removed from the carbon arc lamp house. The interior was finished with dark-gray nonreflecting and heat-resisting paint after this photograph was taken.

The holes in the lamp house appear to provide adequate air circulation. It was possible

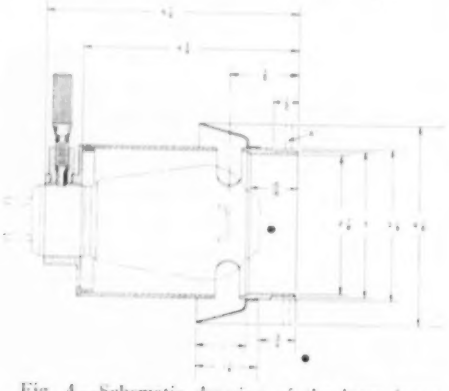


Fig. 4.—Schematic drawing of the lamp house showing the important dimensions.

to touch the lamp house with the bare hand without discomfort after 20 to 30 minutes of continuous operation.

COMMENT

In reviewing the literature on color photography of the fundus, we found that a number of modifications of Zeiss-Nordensen fundus cameras had been designed to adapt them to color film. While any of these modifications might have been applicable to the Bausch & Lomb camera, none of them appeared to be as satisfactory as the zirconium arc lamp (Tower,[4] Catcott,[5] Hansell and Beeson,[1] Ogle and Rucker[6]). Catcott used an incandescent lamp for focusing and an electronic flash tube for the exposure. It was our desire to simplify the modification by using a single light source for both.

Hansell and Beeson's photograph of the human fundus appears to be adequately exposed but suffers somewhat from flatness of detail, possibly because the size of the arc gap (5 mm.) in their xenon tube provided too large a light source. By comparison, the light-source diameter in the zirconium arc lamp is 1.5 mm.

Ogle and Rucker's modification required alterations in the optical system of the camera and replacement of the Kodachrome film by Ektachrome film. After these alterations, the authors found that their electronic flash tube, when operated at maximal efficiency, would still underexpose both of these color films. By using Ektachrome (which they processed themselves), they were able to compensate for this underexposure by overdeveloping about two and a half times. This plan has its merits but is unsuitable for photographers who do not have facilities for their own color-film processing.

An optical system designed specifically for a zirconium arc light source would probably give results superior to those we obtained. We were, however, interested in modifying our existing equipment with the shop facilities available to us and at a minimum of expense. The resulting light source makes satisfactory photographs and has eliminated the disadvantages inherent in the old one. There is still room for improvement, but not enough to justify the expense of constructing a theoretically ideal optical system specifically for the zirconium arc.

After the modified camera had been used successfully for photographing dogs, Drs. L. K. Dahl and B. G. Stall, of the Brookhaven Medical Department, tested it on human patients. The results were closely comparable to those previously obtained with the carbon arc, and the patients were considerably more relaxed. The exposure time for the human retina is one-tenth to one-fifteenth second.

SUMMARY

A zirconium concentrated arc lamp was adapted to the Bausch & Lomb retinal camera, replacing the original carbon arc equipment. The new light source resulted in good photographs of canine and human retinas, with improved modeling of the blood vessels. The zirconium lamp operates silently, is comparatively cool, and gives a uniform brightness and color temperature over a wide variation of input voltage. The equipment required to make the change is a standard power supply unit, a 100-watt zirconium arc lamp, and a lamp house. The first two items are available commercially, and the third can easily be made in a machine shop.

This research was carried out under the auspices of the U. S. Atomic Energy Commission.

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Intraocular Metallic Foreign Bodies Following Cataract Extraction

Report of Seven Cases

ALBERT E. TENNENBAUM, M.D., Chicago

This report describes retained intraocular metallic foreign bodies found in seven eyes after cataract extraction at the Illinois Eye and Ear Infirmary.

The first case was seen in October, 1953, when a golden-colored, metallic-like foreign body was noted deep in the healed corneal wound of a patient who had had cataract surgery one month previously. The following month a similar foreign body was noted lying on the iris in another eye that had persistent, unexplained iritis following an uncomplicated lens extraction. In the following months five additional eyes which had recently been operated on were found to contain similar foreign bodies. In every case a gold-plated Bell erisophake had been used during the operation.

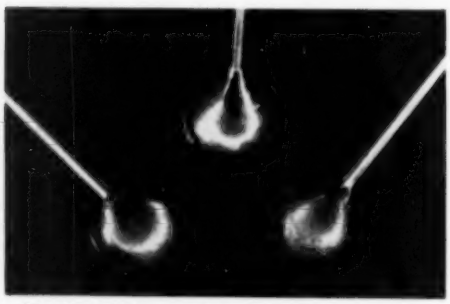

Fig. 1.—Flaking gold plating of the erisophake.

These findings stimulated an investigation of our instruments, which revealed that every gold-plated erisophake used at this institution had a roughened surface, as seen on examination with the naked eye. On examination under high magnification, the uneven surface was found to be due to a flaking off of the gold plating (Fig. 1). In the manufacture of these instruments a plating is applied to a nickel-silver base. Since no other plated instruments were used during the operation, it is likely that the intraocular foreign bodies were from the erisophake plating. No similar flakes have been found after cataract extraction in which a capsule forceps was used. Because of these findings, only nonplated stainless steel erisophakes are now used at the Infirmary.

From the Department of Ophthalmology, Illinois Eye and Ear Infirmary of the University of Illinois College of Medicine.

REPORT OF CASES

Case 1.—White woman, aged 77. Sept. 1, 1953, intracapsular cataract extraction with full iridectomy. Postoperative course uneventful. One month later, a "yellow-brown, metallic foreign body" was noted deep in the healed corneal wound near the temporal suture position. This has produced no inflammatory reaction, and vision was corrected to 20/70.

Case 2.—White man, aged 64. Aug. 20, 1953, intracapsular cataract extraction with full iridectomy and slight loss of vitreous. The eye showed a persistent aqueous flare for five months following surgery, despite treatment with cycloplegics and cortisone topically. Five months after operation, two minute yellowish metallic foreign bodies were seen on the surface of the iris.

Case 3.—White man, aged 70. Nov. 18, 1953, intracapsular cataract extraction with peripheral iridectomy. Postoperative course was uneventful, with corrected vision of 20/20. Study of the anterior segment revealed extensive synechias of the iris to the vitreous face. A single metallic foreign body, golden in color, was noted 1 mm. from the inferior pupillary margin. The eye was free of inflammation.

Case 4.—White man, aged 68. June 4, 1953, intracapsular cataract extraction with peripheral iridectomy. On the first postoperative day a small iris prolapse was noted. This was repaired with an iridectomy and postplaced corneoscleral sutures.

The patient developed a choroidal detachment and flat anterior chamber on the 18th day. This condition subsided spontaneously. The corrected vision was 20/20—1. Slit-lamp examination revealed eight minute gold foreign bodies on the iris surface near the sphincter region. The eye was free of inflammation.

CASE 5.—White man, aged 77. Oct. 3, 1953, intracapsular cataract extraction with peripheral iridectomy. Postoperative course was considered uneventful, and the patient was discharged from

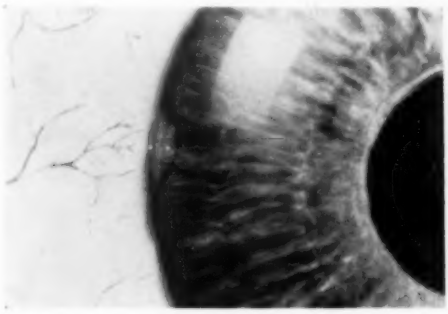

Fig. 2.—Metallic foreign bodies in iris adjacent to synechias.

the hospital on the 10th day. During the third postoperative week a choroidal detachment with a shallow anterior chamber was noted. This subsided without treatment. However, anterior and posterior synechias were noted, with a rather intense iritis. The patient was treated with subconjunctival and topical cortisone. The iritis quickly subsided, and at this time a single metallic foreign body was noted on the iris surface temporally. Six weeks postoperatively a full iridectomy with removal of the foreign body was performed, after which an uneventful recovery was made. Vision was 20/20—2.

CASE 6.—White woman, aged 63. July 1, 1953, intracapsular cataract extraction with full iridectomy and loss of 1 cc. of formed vitreous. A small hyphema was noted on the third postoperative day. This quickly absorbed, and corrected vision is now 20/20—3. Seven months after operation, a small fleck of gold was noted on the surface of the iris temporally. The eye has remained pale.

CASE 7.—White man, aged 70. Oct. 23, 1953, intracapsular cataract extraction with peripheral iridectomy without complication. A low-grade iritis persisted for six months after surgery. Peripheral anterior synechias formed temporally, and two golden foreign bodies were seen adjacent to the synechias. Cortisone was started topically, and the inflammatory reaction gradually subsided (Fig. 2). The eye is now quiet and has received no medication for six weeks. Corrected vision is 20/100—. The macula has a granular appearance, and the central field shows a 5-degree central scotoma.

SUMMARY

Seven cases are described in which flecks of gold instrument plating were found in the anterior segments of eyes from which cataracts had been removed. In all instances a gold-plated erisophake had been used during the procedure. In three of the cases the eyes showed no signs of irritation; in three there was a persistent iritis (vitreous loss occurred in one of these), and in one otherwise uncomplicated extraction extensive posterior synechias had formed. The use of plated erisophakes should be discontinued in favor of stainless steel instruments, which are now available.

109 N. Wabash Ave. (2).

Registry of Interesting Cases

It is the purpose of this section to record cases on the basis of interest only. No complete review of the literature is attempted and no claim for priority is implied except when specifically stated. Publication of case reports is subject to the concurrence of the Editorial Board on the interesting aspects of the case. It is requested that the reports submitted be as brief as is consistent with inclusion of the pertinent facts, bear a title that is as specific as possible, be prefaced by a paragraph that states why the author feels the case is of interest and be accompanied with photographs whenever possible.

CYSTINE DEPOSITS OF CORNEA AND CONJUNCTIVA

CYSTINOSIS is a rare metabolic disease of children in which renal rickets, dwarfism, acidosis, hypophosphatemia, and renal glycosuria are commonly found. The outstanding pathological feature appears to be a universal deposition of cystine crystals throughout cells of the reticuloendothelial system. Among the organs involved are the kidney, spleen, lymph nodes, liver, lung, gastrointestinal tract, thymus, testis, bone marrow, and eye.

The disorder is of a hereditary nature and is associated with metabolic errors of the sulfur-containing amino acids methionine and, especially, cystine. It is thought that the failure in the oxidation of cystine to a sulfate causes the accumulation of unoxidized cystine, much of which is excreted in the urine.

The first case of corneal and conjunctival cystine deposits was reported by Bürki[1] in 1941. On histological examination he found the crystals present not only in the cornea and conjunctiva but also in the uveal tract, sclera, and episclera. About eight additional cases of such eye findings have since been reported in the literature. In most instances the diagnosis was made by slit-lamp examination alone. Characteristically there were myriad crystalline deposits within the conjunctiva and superficial cornea. The history of an additional case which I had the opportunity of observing recently follows.

REPORT OF CASE

D. E., a 2½-year-old mulatto boy, entered Stanford University Hospital on Feb. 1, 1954, with a history of urinary frequency and growth failure of one year's duration. Physical examination; blood count, and blood sugar, protein, cholesterol, sodium, and chloride determinations were within normal limits. The blood urea was 64 mg.; potassium, 3.1 mg.; calcium, 10.0 mg., and phosphorus, 3.5 mg., per 100 cc.; CO_2-combining power, 42 vol.%, and alkaline phosphatase, 12.1 Bodansky units. The urine could not be concentrated to a specific gravity of over 1.004 and showed a 1+ protein reaction (2 gm/24 hours). The Sulkowitch test for urinary calcium was negative. The urinary amino nitrogen amounted to 163 mg/24 hours (normal being 25 mg/24 hours), and the Sullivan test for urinary cystine was strongly positive. The P. S. P. test yielded less than 5% excretion in 15 and 60 minutes. Bone marrow studies showed no abnormalities. X-rays of the ankles were characteristic of rickets.

Examination of the eyes was remarkable in that the bulbar conjunctiva and superficial corneal stroma were infiltrated with small crystals. The deep corneal stroma, anterior chamber, iris, vitreous, and fundus were negative bilaterally. Visual acuity and intraocular pressure were normal. On Feb. 25 microscopic examination of a biopsy specimen of the bulbar conjunctiva revealed many cystine-like crystals. This finding was followed by a special chemical test on the biopsy material. Chromatographic analysis of the dinitrophenyl derivatives of the amino acids present revealed that the only low molecular amino acid in the specimen was cystine. This substance was found in great abundance.

Since his discharge from the hospital, the patient has done well on a regimen designed to correct his electrolyte imbalance. On May 18, 1954, slit-lamp examination showed no change.

Fig. 1.—Widened epiphysial cartilages at the distal ends of the tibia and fibula, with irregularity of the epiphysial plates of the tibia and distal femur, compatible with a diagnosis of rickets.

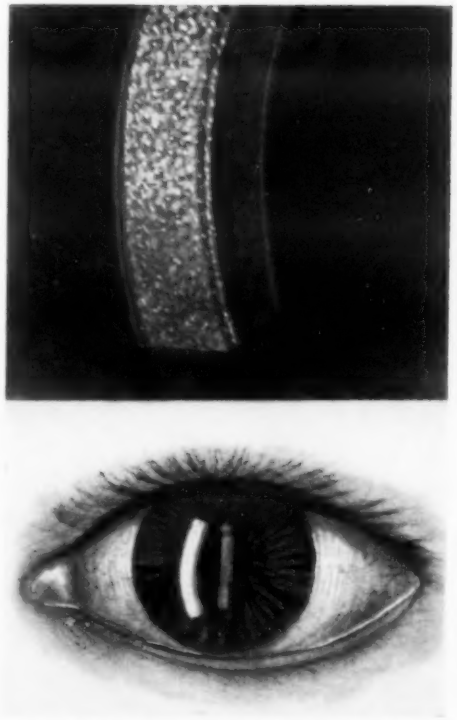

Fig. 2.—Slit-lamp picture of corneal crystalline deposits (courtesy of Dr. Thomas Stevenson).

Fig. 3.—Photomicrograph of the fresh conjunctival biopsy specimen, showing hexagonal crystals which are suggestive of cystine.

Comment.—Although in some of the previously reported cases of ocular cystinosis a chemical analysis of the conjunctival specimen had been made, this case is the first in which chromatographic analysis was used. This method is reliable because the conjunctival proteins cannot interfere in the detection of individual amino acids.

This case, however, is not typical in that cystine deposits were not found in the bone marrow and only small amounts of sugar were detected quantitatively in the urine (600 mg/24 hours). A definite hereditary pattern could not be established. The parents' urinary amino nitrogen was within normal limits.

SUMMARY

A case of ocular cystinosis is presented in which the patient also suffered from cystinuria, renal failure, acidosis, and rickets. The nature of the conjunctival crystalline deposits was established by chromatographic analysis of a biopsy specimen.

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Annual Reviews

DISEASES OF THE UVEAL TRACT

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THIS REVIEW of the important available papers on diseases of the uveal tract covers the period from October, 1953, to October, 1954. Several articles are included which were omitted from the previous annual review. The text will emphasize the reports which, in my opinion, have been the most noteworthy contributions to the advancement of knowledge in this field.

CONGENITAL DEFECTS

Berryman [1] describes the tests to be utilized in the differential diagnosis of anisocoria and reports two new families with congenital anisocoria. He believes that mild degrees of anisocoria are common in otherwise normal persons and that the condition is analogous to facial asymmetry. The familial type can be diagnosed by its paradoxical reaction to epinephrine drops following cocaine. It is inherited as an irregular dominant characteristic, is not associated with other defects, and is without pathological significance.

ANATOMY

Redslob [2] describes his histological studies of the development of the dilator iridis muscle. Although it is commonly accepted, particularly in France, that the dilator muscle is elaborated by the anterior epithelium, Redslob presents evidence for the less accepted view that it is formed by smooth muscle fibers, giving the following as evidence: In the embryo there are nuclei of smooth muscle fibers right inside the lamina; the lamina is separated in certain places from the epithelium by capillaries, sphincter fibers, and heterogeneous cellular elements, making it impossible for the epithelium to elaborate its muscular layer; unstriped muscle fibers leave the dilator to penetrate the stroma; the dilator extends to the ciliary region, often far away from the iris epithelium zone; the minute histological structure of the dilator layer does not look like a myoepithelial formation.

Wybar [3] presents a beautiful study of the choroidal circulation, utilizing Ashton's technique of neoprene latex injection and individual vessel dissection. He demonstrates a free communication at the equator between the anterior and the posterior sets of vessels, in contrast to the previous assumption. The short posterior ciliary arteries, although segmentally arranged, are not connected with one another directly except near the posterior pole of the eye and cannot be regarded as true end-arteries, since each is capable of supplying the whole or part of the choroid by way of its free anatomoses with the anterior choroidal vessels. Wybar also demonstrates that the capillaries of the choriocapillaris are not uniform in caliber or concentration but become smaller and more densely packed as they approach the optic disc. The capillaries underlying the macula do not differ in structure from any similar part of the retina at an equivalent distance from the disc. No arteriovenous anastomoses have been found in any part of the choroid.

Fritz and Bingen [4] present a study to demonstrate that the choroidal and retinal circulations fulfill the same role of supplying the retina despite their different anatomical structures. The two circulations have the same embryonic origin and are fed by branches of a caliber analogous to that of the ophthalmic artery, and equal pressure values are obtained for the retinal and the choroidal arteries, as well as for the cilioretinal arteries. Anatomically, the capillary network of the choroid is more developed

From the Department of Ophthalmology, Emory University School of Medicine.

than its retinal counterpart, occupying 60% of the total volume, as against 10% for the retina; it seems certain, however, that the choroid receives a quantity of blood directly proportional to the volume of its capillaries.

PHARMACOLOGY AND PHYSIOLOGY

De Roetth[5] presents a physiochemical study of the glycolytic activity of the ciliary processes, comparing it to similar activity found in typical secretory glands. It is concluded that from a biochemical point of view the ciliary processes resemble, but are not typical of, other known secretory glands.

Morone[6] studied the amino-oxidase activity of the iris after section of the cervical sympathetic system and found that if the section is carried out at the third neuron of the pupillary pathway there is a reduction in the amino-oxidase activity. If the section is localized at the second neuron, the amino-oxidase activity remains unchanged. These findings might help one to understand the epinephrine-dilator mechanism of the pupil in paralysis of the cervical sympathetic system. Morone[7] also found that the amino-oxidase activity of the iris was stimulated after the instillation of cocaine.

Marconcini[8] demonstrates experimentally that a 1% neutral solution of atropine sulfate in 0.90% sodium chloride produces a greater mydriasis than the atropine sulfate solution without sodium chloride.

Lange,[9] by conducting experiments on the pupils of patients with scopolamine and levoglaucosan (histamine and epinephrine) prior to cataract operation, concludes that the cause of the miosis and pupillary sluggishness in old age is the reduced tonicity of the vegetative nerves innervating the pupillary muscles. The anatomical changes are considered secondary.

Hess[10] describes his comparative physiological and pharmacological studies on the isolated iris of oxen, pigs, rabbits, and cats. In all four species there is a double antagonism, chemical and mechanical, which regulates the width of the pupil.

Using the Zeiss-Opton transscleral illuminator, Ohki[11] studies the fundi with various filters and finds that the green filter is the best for observation of the iris arteries and choroidal vessels. By this technique, and applying pressure with Bailliart's ophthalmodynamometer, he succeeds in measuring the blood pressure of the iris arteries. The minimum pressure was 56.675 ± 0.695 mm. Hg; the maximum was 75.878 ± 0.908 mm. Hg. The maximum blood pressure increases with age; the minimum remains unchanged. The blood pressure falls successively in the iris, anterior ciliary, and central retinal arteries. Using the same method of transscleral illumination, Ohki[12] describes the appearance of certain choroidal lesions.

DEGENERATIVE CONDITIONS

Iridoschisis.—This condition, which usually occurs in elderly people, is reported in a 20-year-old airman by Krohn and Garrett.[13] The patient had noted visual disturbances for three months and was found to have advanced keratoconus and milky-white, complicated cataract. No definite cause for the condition could be assigned.

Essential Atrophy of the Iris.—The most important recent contribution to the knowledge of this condition is the histopathological study of 10 cases by Heath.[14] He demonstrates very clearly multiple vascular occlusions with associated anemic infarctions of the iris, and even the ciliary body. The glaucoma is assumed to be due to the iris atrophy, producing loss of resorption capacity from actual loss of iris tissue, peripheral anterior synechiae, and the blocking effect of accumulated iris debris and detritus in the angle. The absence of inflammatory cell changes and the clinical course are explained by the anemic infarctions. If glaucoma occurs early, the histological characteristic is the presence of cuticular remains impeding the trabeculum. The cause of the local blood vessel disease producing the condition in the iris is not known. To date, there is no explanation for the fact that the condition is unilateral and ocurs more commonly in women. No genetic patterns are found in the cases studied.

INFLAMMATIONS

General Considerations. — According to Berens and Bickerton,[15] national and international statistics reveal that approximately 15% of blind persons lost their vision because of uveitis. These authors point out that the correlations of the clinical and pathological diagnoses are frequently incorrect and that the etiology is impossible to determine in 25% of cases.

Uveitis is a problem of real importance to the military because of the long hospitalization required. Fair [16] analyzes 97 cases of uveitis at the Walter Reed Army Medical Center and finds that cases primarily admitted because of uveitis account for 5% to 10% of all admissions. In these cases a positive Sabin-Feldman dye test for toxoplasmosis in a dilution of 1 : 256 was considered to have some etiological meaning. Fair states that toxoplasmosis as an etiological factor in the uveitis of adults has to be proved or disproved in a combined serological, pathological and isolation study of the patients in question. Leptospirosis was not found to be a common cause of uveitis in military personnel.

In Brazil, Alvaro [17] analyzes 175 cases of uveitis and establishes their etiology as follows: focal causes, 69.21%; tuberculosis, 5.14%; syphilis, 5.71%; lymphogranuloma venereum, 0.57%; unknown causes, 19.37%. In focal uveitis the sources of infection were found to be divided as follows: teeth, 52.57%; tonsils, 43.43%; sinus, 16.57%; intestinal tract, 10.28%; gall bladder, 4.0%; appendix, 3.43%; urogenital tract, 4.57%. Falcone [18] reports on a four-year survey of iridocyclitis in Somaliland and finds that in 592 cases the chief causes were tick-borne relapsing fever and syphilis.

Kimura, Hogan, and Thygeson [19] report the analysis of 47 cases of uveitis occurring in children under 16 years of age. This number represented an incidence in children of 5.8% in their series of 810 cases of uveitis in all age groups. Of the 47 cases, 18 were primarily of anterior uveitis and 29 were primarily of posterior uveitis. Despite extensive studies, an etiological diagnosis was established in only six of the cases of anterior uveitis. Of the 12 undiagnosed cases, an allergic diasthesis was found in 7 and a constant eosinophilia in 2 others, suggesting that allergy may have been an important factor. Of the 29 cases of posterior uveitis, a presumptive diagnosis of toxoplasmosis was made in 10 cases, and 19 cases were undiagnosed. It is noteworthy that tuberculosis was not regarded as responsible for any of the 47 cases in this series. The authors state that in children iridocyclitis from any cause is rare but choriorentinitis is common.

Offret, Saraux, and Bisson [20] present an interesting account of two cases of uveitis with the pathogenic organism in the anterior chamber and give the results of 36 bacteriological investigations of the aqueous humor. In the first case streptococci were cultured from the anterior chamber and the tonsils. In the second case the focus of infection was thought to be in the prostate and Staphylococcus tetragenus was cultured from the aqueous humor. The authors point out the difficulties attaching to bacteriological investigation of the aqueous humor and recommend the following procedure: The specimen should be collected from the centrifugal bottom of the aqueous humor; extreme aseptic precautions should be used; the aqueous should be cultured on bouillon-serum. In the course of the discussion of this paper, Amsler and Verrey expressed similar opinions and gave their own experience to the effect that cultures are positive in 4% of cases of uveitis. An early puncture is more apt to be positive.

Leopold and Dickinson,[21] in a very important contribution, studied 63 cases of uveitis for serum levels of antihyaluronidase and antistreptolysin. They report that the levels tend to be raised in comparison with those for a control group. This study supports the recent work of Woods, who demonstrated a specific hypersensitivity to streptococci in cases of nongranulomatous uveitis. The data presented by these authors suggest that the hemolytic Streptococcus may play an etiological role in the production of uveitis, and that these tests, particularly the antihyaluronidase titer, should be studied further

as a possible method of detecting the etiological agent in cases of uveitis.

Zwiauer, Deutsch, and Streit [22] report that the principal systemic changes in patients suffering from iritis and iridocyclitis are an increased vascular permeability, as demonstrated by the torniquet test; an accelerated sedimentation of the red blood cells, and an increase in the serum globulins.

Remky [23] describes his investigations in cases of iridocyclitis in which a colloid coagulation curve of different dilutions of the aqueous was obtained with the Mastix-Lumbo test. He finds that an abnormal relationship of albumin to globulin persists for a long time, even though the cyclitis seems clinically cured. In measuring the relative concentrations of chloride in the aqueous and in the blood stream, he found that a high chloride concentration is present in the aqueous in chronic uveitis, while in acute inflammations it is low.

Auricchio and Ambrosio [24] find that during the course of iridocyclitis the aqueous and vitreous concentrations of pyruvic and lactic acid are higher than those in the blood, and that there are marked chemical changes in the composition of the lens even while it is clinically intact.

Busacca [25] describes a new phenomenon in the anterior vitreous in cases of uveitis. In watching the movement of the vitreous after the eye moves quickly up and down, this author notes that the vitreous lamellae extend upward, instead of normally falling down again. There is, therefore, a deformity of the plicata of Vogt, with the result that the retrolental triangular space takes on a different shape. The author believes the phenomenon is due to a change in the density of the vitreous.

Vogel [26] describes a method for producing experimental lesions of the fundus in rabbits. He injects into the suprachoroidal space various substances, such as viable cancer tissue, bacteria, and dyes, and believes that rabbits are especially suitable for these experiments.

Schlaegel and Wilson [27] present an interesting experimental study on the mechanism of production of the contralateral uveitis after the use of horse serum in rabbits. The following facts were established: 1. If the eye of a rabbit is injected with horse serum, a granulomatous iritis will develop in the injected eye at about 14 days. 2. If the rabbit has been sensitized previously by intradermal injections of horse serum, uveitis will develop within 1 day, instead of 14, but the contralateral eye remains uninvolved. 3. If after the injection of horse serum into one eye of a normal rabbit, horse serum is given intravenously one to three weeks later, uveitis will develop in the contralateral, untreated eye. 4. The degree of contralateral uveitis is increased by use of the eye, instead of the skin, as a site of sensitization, and it also is increased by the use of large amounts of horse serum intravenously. The authors believe that these experiments, as well as previous ones, support the postulate of systemic antibodies.

Tuberculosis.—Witmer [28] describes his studies with the Middlebrook-Dubos hemagglutination test and serum electrophoresis in patients with ocular disease. The hemagglutination reaction may be a diagnotic aid in ocular tuberculosis only in combination with other clinical findings. Results are positive only at a serum titer of 1:80. In chronic uveitis the aqueous titer corresponds to the serum titer. Parallel determination of the electrophoretic serum fraction and the hemagglutination titer showed in proved general tuberculosis with a high average titer an increase in the alpha and gamma globulins at the cost of the albumin, while in ocular tuberculosis no significant fractional changes in the serum could be determined. Kyosawa [29] studied the same hemagglutination reaction in rabbits and found that the antibody could be demonstrated in the serum and aqueous one and two weeks after inoculation with the tubercle bacilli, and prior to the onset of clinical symptoms and prior to the development of a positive tuberculin reaction. In systemically inoculated animals the antibody appears in the serum and in the secondary aqueous, but not in the primary aqueous. In intraocularly inoculated animals the antibody is demonstrated in the primary aqueous.

The author considers these facts to suggest an intraocular production of antibody. The agglutination titer of the serum is parallel to the severity of inflammation and falls with the use of streptomycin.

Inada [30] finds a decrease in the glucose content of the aqueous in patients with tuberculous eye disease.

Akiya [31] studies the capillary fragility in tuberculous eye diseases by means of the Rumpel-Leede and Borbely tests, finding them positive in about one-half of the cases of ocular tuberculosis, as compared with positive tests in one-sixth of the cases in the control group.

Imaizumi [32] analyzes 1,668 cases of ocular tuberculosis and finds that the condition was bilateral in 888 cases, or 53%.

In a long monograph on ocular tuberculosis, Paufique, Brun, and Bonnet [33] describe the common type of ocular involvement as an allergic reaction to a long-healed systemic infection. This the authors have termed "paraganglionic tuberculosis," in view of the presumptive origin, sometimes from a healed pulmonary lesion but more frequently from subclinical infection of a lymph node, particularly in the mediastinum. The usual manifestations of this type of tuberculosis occur in the mesodermal tissues of the corneal stroma, the uveal tract, the joint capsules, and the skin.

Saggese [34] analyzes the fundus changes in 47 children with tuberculous meningitis and finds that the lesions are always choroidal or in the optic nerve and that hyperemia of the disc and papilledema are four times as frequent as the choroidal lesions.

In 29 cases of amblyopia seen during or after tuberculous meningitis, Esente [35] gave cortisone for one to five months by the general or the retrobulbar route. The cases with chiasmal arachnoiditis showed improvement in vision. The author believes that cortisone is contraindicated in miliary tuberculosis. Lepri [36] finds that cortisone is especially helpful in "paratuberculous" diseases of the anterior part of the eye. According to this author, cortisone may be used with care in granulomatous ocular tuberculosis if combined with antibiotics or chemotherapeutic agents. Cortisone does not interfere with these agents, and in some cases enhances their activity.

Zintz and Wegner [37] report good results with isoniazid (Neoteben) in in vivo and in vitro tests against the tubercle bacillus, but clinical trial with the drug in 85 cases of chronic recurrent ocular tuberculosis was disappointing.

Mishustina [38] describes the beneficial effect of streptomycin in a large number of cases of tuberculous uveitis, and Protopopoff and Dobrotino [39] find that the combination of streptomycin and paraamino salicylic acid was even more effective.

Selye [40] has previously found that pituitary growth hormone administered to tuberculous rats inhibited proliferation of organisms, encouraged granuloma formations, and in general reduced total infection in the tuberculous animal, suggesting that the hormone was capable of increasing the host's ability to produce specific defenses against the infection. Bunn and Robinson [41] repeated these experiments on ocular tuberculosis of rabbits but found no demonstrable effects upon the course of the infection.

During the past year an increasing number of reports have appeared on the experimental and clinical use of isonicotinic acid hydazide (isoniazid) in the treatment of ocular tuberculosis. Woods, Becker, and Wood [42] found that the drug had a marked inhibitory, as well as therapeutic, effect in the tuberculous ocular lesions of rabbits, due to its bacteriostatic rather than its bactericidal, reaction. These authors find a definite tendency for the treated animals to develop a bacillary resistance to the drug and suggest that in the treatment of ocular tuberculosis isoniazid should be combined with streptomycin and some adjuvant drug. Knapp and von Sallmann [43] studied the effect of isoniazid on 75 nonimmune allergic rabbits with ocular tuberculosis and found it to be an effective antituberculous drug both in preventing and in treating experimental ocular tuberculosis. These authors emphasize the necessity of continuing the treatment beyond the clinical

cure, as histological changes and tubercle bacilli can be demonstrated in quiescent eyes.

An excellent article by Schlaegel and Hungerford [44] summarizes the present knowledge concerning isoniazid in the treatment of ocular tuberculosis and describes the results in 22 clinical cases. They find that the drug is relatively nontoxic, passes readily across the blood-aqueous barrier, and is easy and economical to take in tablet form. The recommended dosage is 3 to 5 mg. per kilogram per day, with continuation of therapy for several months after evidence of activity has ceased. They recommend that the drug be used in conjunction with other antituberculosis measures, such as streptomycin and dihydrostreptomycin, PAS, tuberculin desensitization, and rest.

By far the most outstanding paper of the year on ocular tuberculosis is Wood's "Pathogenesis and Treatment of Ocular Tuberculosis," [45] given as the 16th de Schweinitz Memorial Lecture. The years of laboratory research and clinical experience of this authority on the subject are summarized in such a concise manner and the details of diagnosis and modern treatment are so plainly outlined that every ophthalmologist should read and study this splendid contribution.

Toxoplasmosis.—There is currently a great interest in the study of human toxoplasmosis, especially in its possibility as an acquired disease in the adult and in its relationship to certain forms of uveitis. There have been several significant developments in this subject during the past year.

Of the many reports on congenital toxoplasmosis, Glees [46] describes the clinical and histological findings in a case with bilateral microphthalmos. The presence of a choroidal angioma was an additional finding in one eye. The author states that microphthalmos is a fairly common finding in infants dying of congenital toxoplasmosis during the first year of life. Lavat [47] analyzes 20 cases of toxoplasmosis. In addition to the frequent occurrence of chorioretinitis, microphthalmos, nystagmus, and ocular movement anomalies, the author finds that iridocyclitis is not rare. Hill [48] reports a proved case in a 10-month-old child who had persistent pupillary membrane, chorioretinitis, optic atrophy, microcephaly, and mental retardation. Long [49] describes a 13-year-old girl who at the age of 10 months was found to have the characteristic fundus picture. The patient's skull x-rays showed the characteristic intracranial calcifications, and the dye tests were positive in patient and mother. Masters [50] reports a series of five infants with congenital toxoplasmosis and gives a valuable summary of knowledge concerning this disease.

More evidence is accumulating that primary chorioretinitis can occur in the adult from Toxoplasma infection. A probable case is that of a 35-year-old man reported by Hudson.[51] The Toxoplasma serum tests were thought to be diagnostic. Woods, Jacobs, Wood, and Cook [52] present the study, by means of the dye test, of the serums of a large number of cases of nongranulomatous and granulomatous uveitis. The "positive" dye standard used by these authors was a titer of 1:8 or over in children below 10 years; of 1:32 or over for patients from 10 to 19 years of age, and of 1:64 or over for patients over 20 years of age. Using this standard, they found that of 98 cases of nonuveitis controls, 25% had a positive test; that of 110 cases of nongranulomatous uveitis, 25% had a positive test, and that of 201 cases of granulomatous uveitis, 45% had a positive skin test. Assuming that the titers used for a positive dye test are a reliable indication of a Toxoplasma infection, the authors conclude that these studies are corroborative evidence that many cases of granulomatous uveitis are caused by Toxoplasma parasites.

The ultimate isolation and identification of live parasites from a typical clinical case of adult chorioretinitis is presented by Jacobs, Fair, and Bickerton.[53] In this particular case the identification of the organism and its causative relation to the disease are established beyond any question. These authors discuss the confusing fluctuations of titer which occurred in their patient, as well as in some previously reported cases. The

authors confirm the findings of Woods and his associates that toxoplasmin skin testing does not in itself change the serum dye test titer, although previous authors had suggested otherwise.

Experimentally, Beverley, Beattie, and Fry [54] produced uveitis in rabbits and studied the effect of DDS (4:4'-diaminodiphenylsulfone) on the infection. They find that DDS alone caused a regression of the infection, but not of a secondary iritis. When DDS was given with cortisone, which blocked the secondary iritis, complete cure resulted. These authors conclude that this dye should be tried in human toxoplasmosis. Summers [55] finds that Daraprim (2,4-diamino-5-*p*-chlorophenyl-6-ethylpyrimidine) is effective in experimental toxoplasmosis. Its effect in the human infection awaits clinical trial.

Relapsing Iridocyclitis with Mucocutaneous Lesions (Behcet's Disease).—Several additional cases have been reported of this condition, which is thought to be rare in America but rather prevalent in the Eastern Mediterranean region. Adamantiades [56] reports three cases, all of males, in which the triad of symptoms eventually developed: (*a*) recurrent uveitis with hypopyon, (*b*) aphthae of the mouth, and (*c*) ulceration of the sexual organs. He emphasizes that the symptoms may often appear separately and that several years may elapse between the development of each symptom. He also emphasizes that recurrences of each symptom are common. Moodie [57] reports four cases, and Calmettes, Deodati, Basex, and Amalric [58] describe the condition in a 4-year-old child who had retinal hemorrhages associated with typical recurrent uveitis. Huerkamp [59] states that only one case has been reported in which the uveitis and hypopyon were unilateral. He describes a case with recurrent unilateral uveitis and hypopyon which followed the magnet extraction of an intraocular foreign body. The patient developed generalized multiform exudative erythema but had no aphthae of the mouth or ulceration of the genitalia. Bishay [60] describes a case successfully treated with tuberculin injections and local and systemic cortisone. Martin [61] describes the case of a young woman who had the typical triad of symptoms. Treatment with tuberculin desensitization, antihistamines, smallpox vaccine, salicylates, fever therapy, corticotropin and cortisone, and various antibiotics, all gave the illusion of helping at first, due to the spontaneous regression of each episode. In a very interesting paper, François [62] outlines the clinical manifestations of polymorphous erythema, Stevens-Johnson syndrome, Behcet's syndrome, and Reiter's syndrome. He believes that there is a relationship of these different diseases but that a common causal agent has not yet been found. He recommends the term "pluriorificial erosive ectodermatosis," instead of "ocular mucous membrane syndrome" (Robinson) or "mucous-cutaneous syndrome" (Nutt).

Uveitis Associated with Joint Disease.—Davis,[63] in a study of 10 cases of active anterior uveitis in children under 16 years of age, reports the presence of rheumatoid arthritis in 4 cases and the history of arthritis without residual deformity in 2 cases. In neither of the latter was there any sign of active or inactive rheumatic fever. No other etiological factor was found in any of these patients, except for sarcoidosis in one. For the remaining 4 patients the etiology was undetermined. Davis finds 56 previously reported cases of children demonstrating the triad of band-shaped keratopathy, iridocylitis, and rheumtaoid arthritis (Still's disease). In his interesting discussion of the band keratopathy in this syndrome, Davis states that the keratopathy is apparently peculiar to juvenile arthritis and has not been noted as commonly in cases of adult iritis associated with rheumatoid arthritis. The keratopathy is probably secondary to the iridocyclitis and appears while the eye is yet relatively undamaged by the iritis, in contrast to band keratopathy secondary to iritis in adults. The author states, further, that the probable cause of the band keratopathy in these cases is the disturbed aqueous physiology produced by the iridocyclitis, which leads to impaired nutrition of the cornea, predisposing it to

calcific degeneration. The blood calcium level is usually normal in these cases. An uneventful intracapsular extraction of a complicated cataract was performed in one case, but the eye became atrophic and light projection faulty, a common outcome in such cases.

Von Wolffersdorff [64] reviews the clinical course of Still's disease and its ocular complications and reports the case of a child who had been treated for tuberculous arthritis until the typical ocular complications of Still's disease appeared, leading to further evaluation and a change in the original diagnosis. The general and ocular condition improved after tonsillectomy and antibiotic therapy.

Unger and Schomerus [65] analyze 19 cases of band keratopathy associated with iridocyclitis in children, finding that the joints were involved in only 8. Some of these were considered to be tuberculous, and none could be regarded as cases of typical Still's disease. The authors conclude that the band keratopathy after iridocyclitis is not pathognomonic for Still's disease.

In discussing the ocular manifestations which occur in 20% of chronic rheumatism in childhood, Lavat [66] is unable to say with certainty that there is a specific form of rheumatism which determines the ophthalmological syndrome. He emphasizes that these ocular manifestations (iridocyclitis, band keratopathy, and complicated cataract) are insidious in onset, are always bilateral, and are frequently not recognized until late.

In reporting two cases of iritis associated with gout, Bonamour [67] emphasizes that this type of iritis is always acute, severe, and unilateral and that the anterior chamber contains much exudate and blood. Treatment with colchicine gives complete and rapid recovery.

Leptospiral Uveitis.—There is an increase in the number of reports of this type of uveitis from the European countries, where human leptospiral infection is commoner than in the United States. Moro [68] reviews the literature to date and gives a detailed report of 17 cases. He finds that ocular involvement is commonest in males and in the second decade of life. The ocular infection was unilateral in 7 cases and bilateral in 10 cases. When bilateral, it appears in the two eyes simultaneously. The onset is during or following the symptoms of general infection and may be either an anterior uveitis or generalized uveitis. The anterior uveitis may be an acute serous or serofibrinous iridocyclitis or a latent, quiet cyclitis. It may heal in a short time, or it may recur and take a chronic form, with extension to the choroid, retina, and optic nerve. The chronic total uveal involvement must be carefully differentiated from tuberculous uveitis; a slow evolution and marked alteration of the vitreous body are characteristic of leptospiral uveitis. The general symptoms may be mild. The diagnosis is established by serological examination of the aqueous and blood. The most frequent agent responsible for the ocular infection is Leptospira icterohaemorrhagica; then L. pomona, L. canicola, and L. bataviae.

Stergar and Novak,[69] in reporting two cases due to Australian leptospirosis A, emphasize two distinctive signs: (1) the sheathing of veins in the neighborhood of the disc, and (2) the presence of streamer-like exudative formations floating in the vitreous in front of the temporal part of the disc. Riemer's case [70] showed similar unusual formations in the vitreous, as depicted in the author's drawings. Krasishkova [71] emphasizes that the eye may be involved when the general infection has been terminated, and that the retina and optic nerve are frequently involved.

Witmer,[72] in a study on periodic ophthalmia in horses, reports that agglutination titers of the serum and aqueous support the suggestion that the disease is a local leptospiral infection rather than a systemic one. The antibodies responsible for the agglutination titers are contained in the gamma globulin fraction in both serum and aqueous humor. The antibody titer of the aqueous is not related to the number of cells pressent in the aqueous.

Sympathetic Ophthalmia.—Schreck [73] reports a new series of experiments performed on monkeys. From an egg membrane culture of an organism isolated from a human

case of sympathetic ophthalmia, he inoculated the right eye of two monkeys. The first monkey developed a severe plastic uveitis in the right eye one week later and in the left eye five weeks later. Periodic inoculation of egg membrane with the aqueous from each eye produced a pure growth of the original organism in four out of five tests on the right eye and in two out of two tests on the left eye. Histological examination of the eyes and of the visual pathways showed the same previously described periangiitis and perineuritis migrans in the optic nerves, chiasm, uvea of both eyes, and orbital tissues. The histological sections showed the same microorganism as that found in the egg cultures. The second monkey so inoculated showed a transient uveitis in the injected eye but no reaction in the left eye. Cultures of the aqueous showed no growth on egg membrane. A third monkey received an inoculation of aqueous from a clinical case of sympathetic ophthalmia, but both eyes remained free of inflammation. A fourth monkey received in the right eye an injection of pulverized uveal tissue from a clinical case of sympathetic ophthalmia. After a latent period of two weeks, the right eye developed a chronic uveitis, which healed after three months. During this time the left eye remained free of inflammation as examined with the slit lamp. The histopathological signs were the same as those in the first monkey, but there was only mild involvement of the left. Periodic inoculations of egg membrane with aqueous from each eye were positive in one out of eight tests in the right eye and in two out of eight tests in the left eye. The fifth monkey received an injection into the right eye of a pure egg culture made from the human material used in the fourth monkey. A plastic iridocyclitis apeared in the right eye in 3 weeks and in the left eye 10 days later. Periodic inoculations of egg membrane with the aqueous from these eyes were positive in two out of five tests in the right eye and in three out of five tests in the left eye. The histopathologic findings were characteristic and similar to those found in the first monkey.

Schreck states that these experiments in monkeys confirm his previous work on chickens and prove his ability to transmit the causative organism to the experimental animal, where it produces a sympathetic inflammation of both eyes.

Oesterle [74] could not duplicate Schreck's results in chickens. When he inoculated material from human cases into chicken eyes, a lymphocytic infiltration in the second, noninoculated eye occurred after two weeks to six months. No infiltration was found in the optic nerve or chiasm, and no specific micro-organisms could be found. When the inoculations were made with material from eyes free of sympathetic ophthalmitis, similar results were obtained. In the discussion of the work, Schreck spoke of the technical difficulties of his method, especially in the careful preparation of material and in egg inoculation.

Reports of cases of sympathetic ophthalmia are given by Santos,[75] Ribalskaya,[76] Senal,[77] and Druault-Toufesco.[78] Guest,[79] and also Pola and Moren,[80] report new cases and emphasize the fact that many cases of so-called sympathetic ophthalmia following cataract extraction are in reality other pathological processes, probably phacoanaphylactic uveitis. Guest believes that the latter group is the one which, in general, makes the most dramatic response to cortisone therapy. Letson [81] reports a case of sympathetic ophthalmia following a basal iridectomy, and Kornblueth and Stein [82] give the details of the first reported case of sympathetic ophthalmia following operation for retinal detachment. The operation consisted of surface and penetrating diathermy but failed to reattach the retina. A late complication, consisting of an orbital cellulitis, was relieved by antibiotic therapy. Ten months postoperatively the opposite eye became inflamed. The diagnosis was confirmed by histological examination of the sympathogenic eye.

Fukuda [83] finds that in patients in the convalescent stage of sympathetic ophthalmitis there is an increase in the keto-enol substance in the urine and that this occurs in Harada's disease also. Lavat [84] presents a

review of theories concerning the origin of sympathetic ophthalmitis.

Syndromes of Harada and Vogt-Koyanagi.—Remky [85] describes three patients with uveoencephalitis. Aqueous and cerebrospinal fluid from one of these patients were injected into the vitreous of rabbit eyes, producing a serous chorioretinitis. The chorioretinitis produced by the injection of aqueous humor was not further transmissible, but that produced by the injection of cerebrospinal fluid was transmissible through five passages. Injection of the aqueous of affected animals into the anterior chamber in other animals caused a violent anterior uveitis; further inoculation of aqueous from animals thus affected into the vitreous body in other animals caused chorioretinitis. Attempts to isolate the pathogenic agent by inoculation of egg membrane, mice, and guinea pigs were inconclusive. Remky analyzes 116 cases of uveoencephalitis collected from the literature and shows that meningeal signs are rarely absent when there is retinal detachment; that the presence of chorioretinitis is associated with meningeal signs plus depigmentation of the hair and skin, and that meningeal signs do not occur in anterior uveitis, but disturbances in pigmentation are invariable.

Stadnik and McFadden [86] report a case of Harada's disease with bilateral retinal detachment, signs of meningeal irritation, dysacousia, vitiligo, poliosis, and pleocytosis of the spinal fluid. Injections of the spinal fluid into the vitreous of four rabbit eyes showed only transient inflammatory reaction and negative histological examination of the enucleated eyes. The ocular condition became worse on systemic cortisone but improved on sodium salicylate therapy for three weeks, penicillin for four days, and one injection of gamma globulin.

Crawford [87] reports a case in which cortisone was used in the early stages. The immediate result was dramatic, but when the disease recrudesced, the drug became ineffective. He advises continuing cortisone a long time to achieve cure.

Other cases of uveoencephalitis, either of the Harada disease type or showing the Vogt-Koyanagi syndrome, are reported by French,[88] Fabie,[89] Soliman,[90] Zarrabi,[91] Torres,[92] and Puig Solanes.[93] Carreras, Gilsamz, Palacios, and Goytre [94] report two cases of the Vogt-Koyanagi syndrome, one of them probably due to toxoplasmosis.

Heterochromic Cyclitis.—Paufique and Chavanne [95] emphasize the diagnostic value of the Amsler and Verrey sign in Fuchs's heterochromia. Only in this condition does anterior chamber puncture produce a small hemorrhage in the iridocorneal angle opposite the site of the puncture. Calmettes, Deodati, and Amalric [96] describe an interesting case in which Horner's syndrome followed stellate ganglionectomy, and heterochromic cyclitis developed in the same eye on the same date. Vannini [97] analyzes the gonioscopic findings in heterochromia iridis. Of 15 cases of Fuchs's heterochromia, 8 showed a normal corneoscleral angle, 3 showed numerous vessels, and 4 showed numerous vessels and congenital anomalies. The fellow eye was normal in very case. Of three other cases of heterochromia of neurogenic origin, the angle was normal in one; anomalies of the angle in a sector corresponding to the discoloration were shown in the others. François [98] gives an excellent review of the entire subject of Fuchs's heterochromia. He analyzes a large number of cases and finds that the condition is rarely bilateral, that the aqueous is usually clear, but that keratic precipitates and cataract are invariably present. There is always present a hypochromia of the iris and atrophy of the pigment border of the iris. Gonioscopy is often negative, and posterior synechiae are never present. François believes that the Amsler and Verrey phenomenon, as well as his histopathological study of two cases, shows that the changes are of a degenerative nature, and not inflammatory. He believes that the condition is produced by paresis of the cervical sympathetic nerve supply. As evidence, he describes the following tests. In Fuchs's heterochromia, cocaine dilates the affected pupil slightly, but epinephrine does not. When the two drugs are given together, dilatation is better than with cocaine alone.

When amphetamine (Benzedrine), 1% solution, is instilled into both eyes, the pupil in the heterochromic eye dilates more slowly and less widely than that in the fellow eye.

Miscellaneous Inflammations.— Cases of retinochoroiditis juxtapapillaris (Jensen) are reported by several authors. Pagliarani [99] describes nine cases treated by calcium, vitamins, and x-ray therapy. He believes the disease is relatively benign but tends to relapse. Marsico [100] describes a case which seemed to be related to a dental infection. Bruna [101] reports three cases in which the relapses were severe and prolonged, suggesting a peculiar reaction in the uveal tract sensitized by the previous localization of the disease. In a case of Wittich [102] the inflammation produced an obstruction of a cilioretinal artery by compression.

Endophthalmitis phacoanaphylactica following the removal of a magnetic foreign body via the anterior route is described by Berche and Berche.[103] The treatment consisted of promethazine (Phenergan) and intravenous calcium. Scheffler [104] gives an interesting clinicopathological case report of typical endophthalmitis phacoanaphylactica in which there was a superimposed granulomatous iritis. Such a combination has not been reported previously.

Occurrence of iritis and glaucoma in a case of mumps is reported by Riffenburgh,[105] who finds that the eye involvement was mild and self-limited. Kirber and Kirber [106] report on experiments in which they produced a fibrinous iritis and keratitis in guinea pigs by injecting the Enders strain of mumps virus into the anterior chamber. These animals developed high antibody titers against mumps antigens. In discussing this paper, Henle * suggests that serological tests for mumps should be performed in some cases of iritis, even though there is no accompanying parotitis, since it is now known that the so-called complications of mumps, such as meningoencephalitis and orchitis, are frequently part of the primary picture of the disease, and on occasion may be the only sign of the infection.

Brucellosis with involvement of the eye has not previously been described in Great Britain, according to Foggitt,[107] who reports a case with transient mild iritis in one eye and progressive retinal periphlebitis, appearing 14 months later, in the other eye. A brucellin skin test was strongly positive, and the agglutination titer was positive in 1 : 120 dilution. Foggitt states that the skin test is suggestive of the diagnosis if positive, but if negative the patient still may have brucellosis. He advises drawing blood for the serum agglutination titer at the time of the skin test. A sharp rise two weeks later is diagnostic. If there still is doubt, a liver biopsy will establish or rule out the diagnosis.

A case of meningoencephalitis and uveoretinitis due to herpetic virus is reported by Schiff-Wertheimer, Fortier, and Maria.[108] On the day following the removal of a corneal foreign body, a 30-year-old man developed severe uveitis and retinal vascular thrombosis. Five days later the fellow eye became involved and presented papilledema, hemorrhages, and macular edema. There was a pleocytosis of the aqueous and cerebrospinal fluid. A virus (probably herpetic) was isolated from the cerebrospinal fluid.

Torulosis with ocular involvement is reported by Wager and Calhoun,[109] who found in the literature three previously reported cases and described a fourth. All patients had central nervous system signs, and all died.

Therapy of Uveitis.—Agarwal and Raizada [110] report on the usefulness of the drug Irgapyrin in a wide variety of ocular inflammations. Irgapyrin is a new pyrazole derivative formed by the combination of amiopyrine and phenylbutazone (Butazolidin). The drug has an analgesic, antipyretic, and anti-inflammatory action, with a low toxicity. Harmuth [111] presents the results in 18 cases of iridocyclitis treated with injections of Irgapyrin. The drug is well tolerated, even by older patients, and is most beneficial in spontaneous or postoperative serous iridocyclitis. Kamel [112] describes the beneficial

* Henle, W., in discussion on Kirber and Kirber.[106]

effects of Irgapyrin in cases of iritis following cataract extraction, some treated with 2 to 10 intramuscular injections and some with tablets. All cases were cured, but no effect was obtained in the iritis of Behcet's disease.

Alvaro [113] reviews the literature on the x-ray treatment of uveitis and gives the results of his animal experiments. He produced an experimental nongranulomatous uveitis in guinea pigs and treated the eyes with x-rays. The uveitis subsided more quickly in the treated cases than in the untreated controls. Treatment consisted of medium hard x-rays in a dosage of 80 to 100 r, filtered through 0.5 mm. Cu and 0.5 mm. Al, with a skin-target distance of 33 cm. Treatment was divided into four exposures. Results were better in anterior than in posterior uveitis, and the beneficial effects are ascribed primarily to vasodilatation.

Di Marzio and Strazzi [114] analyze the results in 880 cases of uveitis treated with x-rays. Of these patients, 410 recovered, 316 improved, and 154 were failures. The authors' technique was to give four to six applications of 120 r at five- to six-day intervals, using hard rays with a skin-target distance of 30 cm. Treatment was given with a 5 cm. portal, the cylinder resting on the bony orbital rim and the eye being closed. Although the authors had no control series, they believed that x-ray therapy was valuable in all types of uveitis and often effected a cure when other treatment failed. No harmful effect, particularly cataract, was ever produced. Tuberculous uveitis responded best; syphilitic uveitis, less rapidly, and the rheumatic types, even more slowly.

Fried [115] describes the clinical results in 340 patients with various forms of uveitis treated with small doses of x-rays (40 to 60 r). The usual treatment was four exposures of 40 r at intervals of four days. Recurrent cases had an interval of three months before renewing treatment, and with this technique no lens damage was seen. Results were better in the treated group than in a smaller group of untreated (control) patients. Experimentally, Fried produced uveitis in guinea pigs in various ways. He found that the inflammations treated with x-rays disappeared more quickly than inflammations in the untreated controls. He also showed ophthalmoscopically and histologically that x-ray therapy produced considerable choroidal vascular dilatation, which persisted as long as two days in some cases. Fried strongly recommends more general use of x-rays in the treatment of uveitis.

Retrociliary nonpenetrating diathermy in the treatment of hypertensive uveitis is discussed by Bartholomé,[116] who finds it a simple, innocuous procedure. The effect of the operation can be strengthened by the use of retrobulbar alcohol injection or by paracentesis of the anterior chamber. The occasional corneal changes that occur after the operation disappear without treatment.

Sivasubramaniam and Hoole [117] treated a hernia of the choroid by scleral grafting, followed by direct suturing of the sclera.

Chandler [118] treats an updrawn pupil by making a keratome incision from below upward and just below the center of the cornea. The iris is grasped with iris forceps without teeth and a small iridectomy performed.

Atkinson [119] recommends the Kuhnt operation for producing an artificial pupil in cases of pupillary obliteration and describes the results in five patients.

CYSTS AND TUMORS OF IRIS AND CILIARY BODY

Cysts.—Politzer [120] has found small vesicles on the anterior border of the optic cup in studying serial sections from human embryonic eyes and suggests that these may explain the origin of spontaneous iris cysts in the adult. Abraham [121] reports the development of iris cysts in 42 out of 66 children receiving isofluorophosphate (DFP). Upon discontinuance of the miotic, the cysts shrink and disappear as rapidly as they had developed. Swan [122] has seen six patients in whom these nodules developed with miotics to such an extent that vision was temporarily obstructed. He also has found two patients in whom such a cyst broke loose and settled in the iris stroma below. Scheie [123] brings to our attention the remarkable value of gonioscopic examination with the dilated pupil for studying tumors and cysts which en-

croach upon the posterior chamber of the eye. The commonest space-taking lesions here are the intraepithelial cysts of the iris or ciliary body, which have a characteristic appearance. Those of the ciliary body are smooth and transparent; those of the iris are covered by pigmented epithelium and appear dark. Malignant melanomas have a more granular surface and show a strong tendency to invade the root of the iris and the anterior chamber.

Proliferations.—Fuchs [124] discusses 10 histologically studied eyes in which there were proliferative nodules in the iris, consisting mainly of large endothelial cells occupying particularly the pupillary area. He considers these to be granulomata rather than naevi vasculosi.

Metastatic Tumors.—Borner [125] and Nover and Schmidt [126] describe cases of mammary carcinoma which metastasized to the anterior surface of the iris.

Melanomas.—Szekler [127] reminds us of the similarity between melanomas of the iris and neurofibromata when he reports a patient who developed melanuria and metastases in the liver after delaying treatment for a melanoma of the iris. This patient had Recklinghausen's disease, a condition which is often associated with benign neurofibromata of the iris. Georgariou [128] reiterates the importance of recurrent hyphema in the diagnosis of melanoma of the iris, a feature well emphasized last year by Esposito.[129] Bangerter [130] removed a malignant melanoma of the iris by performing an iridectomy and excising a portion of the ciliary body at the same time. Fortunately, malignant melanoma of the iris does not occur often in patients with only one eye. Safar [131] reports such a case in which he removed the tumor successfully with electrosurgery, although glaucoma developed postoperatively. Koenig [132] reports an epithelioid cell melanoma in the iris of a one-eyed patient who was under observation for 20 years; there was no postmortem evidence of metastases. Hope-Robertson [133] is interested in the influence of puberty on malignant processes and he describes two patients: a boy of 11 years with a benign nevus of the iris and a man of 28 years with a malignant melanoma of the iris which seemed to begin growing when he was 17 years old.

TUMORS OF THE CHOROID

Unusual Tumors.—Cook [134] reports an interesting patient with ocular and orbital lymphosarcomatous infiltration who seemed perfectly normal two years after enucleation and x-ray treatment of the socket. Müller [135] followed a man with a neuroectodermal tumor which first appeared as a chorioretinitis. Dufour [136] reports an angioma of the choroid which so resembled a malignant melanoma that the eye was enucleated. There was a localized detachment of the retina which could be transilluminated only poorly. The lesion was located in the macular area, and hemorrhages were visible over it.

Metastatic Tumors.—Metastatic carcinoma of the choroid is still comparatively rare. Greer [137] found only 40 undoubted cases in the records of the Institute of Ophthalmology in London for the years 1935 to 1953. In this same period there were 236 cases of retinoblastoma and 1274 cases of malignant melanoma of the choroid. Cases of metastatic carcinoma to the choroid are reported this year by Beauvieux [138]; Appelmans, Dehoux, and Michiels [139]; Maxwell,[140] and Haft and Worken.[141] Sitchevska [142] gives an interesting discussion of the differential diagnosis of carcinoma and malignant melanoma: Carcinoma may cause pain early, but glaucoma occurs comparatively late. It grows rapidly, is flat, spreading laterally; its margins are poorly defined, its color being grayish-pink or yellow. The typical malignant melanoma is painless until the development of glaucoma; it is circumscribed and produces a greater elevation of the retina. Transillumination is more likely to present a shadow with the melanoma. Cogan and Kuwabara [143] provide a valuable study of a patient treated for metastases following breast carcinoma. A lesion in the lung and the choroid increased despite treatment with testosterone, but with diethylstilbestrol there

was marked clinical resolution. The improvement persisted for two years; then active carcinoma appeared in the lungs and abdomen. Metastatic nodules developed in the iris, although the original tumor site in the choroid remained flat. The eye was enucleated and found to contain proliferating carcinoma in the anterior chamber, apparently coming from the iris, and a diffuse carcinomatosis throughout the entire choroid, but relatively sparing the site of the original metastasis in the eye. Zoldan [144] describes an instance of bilateral ocular metastasis of a breast carcinoma in a 40-year-old woman. One eye was surgically removed, and the other was treated with x-rays. Follow-up of three years revealed clinical recovery in the remaining eye, and no other metastases were found elsewhere in the body.

Melanoma.—White [145] warns us to be always alert for the presence of a malignant melanoma, and he mentions such a case which was overlooked by the first ophthalmologist who saw the patient and merely prescribed glasses. Schirren [146] reports the generalized late metastasis of a malignant melanoma of the choroid after 13 years. Strampelli [147] discusses the differential diagnosis of Schwann's uveal melanoma and stromal uveal melanoma. Samuels [148] describes the histological findings of a melanotic sarcoma in a case of sector-shaped melanosis. This tumor showed no relation to the hypertrophic choroidal pigment, and actually had less pigmentation than the choroid. De Veer [149] reports a study of malignant melanomas adjoining the optic disc. It is his opinion that these neoplasms probably never arise from the papilla.

François and Rabaey [150] believe that the basophile content may give a direct indication of the malignity of a uveal melanoma.

Rones and Linger [151] contribute very useful facts to aid in the ophthalmoscopic differentiation of serous detachments and tumorous detachments at the posterior pole of the eye. Cystoid degeneration of the overlying retina may suggest a melanoma. If the tumor breaks through the retina into the vitreous, its irregular surface and the presence of hemorrhages or new blood vessels should point to the diagnosis. MacRae [152] has made a detailed study of 61 cases of malignant melanoma involving the choroid or ciliary body, followed for over five years. His figures suggest that women tend to develop the disease earlier in life than men and that in women it is a less deadly disease than in men. In the group of men there were 57.6% metastatic deaths, whereas in the group of women there were only 31.4%. It is generally true that the heavier the pigment in a malignant melanoma, the worse is the prognosis. Ocular hypotension must not be considered as corroborative evidence of a simple detachment. If histological study reveals a rarity of branched pigment cells, then the prognosis should be comparatively good.

Diagnostic Procedures.—Impressive advances are being made in the use of radioactive isotopes in the diagnosis of tumors of the uveal tract. At last, Thomas, Krohmer, and Storaasli † have devised a Geiger counter which can be applied to any part of the globe, thus overcoming one of the difficulties in the diagnosis of posterior pole lesions, noted by Bettman and Fellows.[155] When radioactive phosphorus, or P^{32}, is injected intravenously, it is metabolized by the tissues, and its concentration in various parts of the eye can be measured by application of the Geiger counter, the tumor, of course, metabolizing a greater amount of the element. This method is advocated only as an adjunct to careful clinical evaluation. Eisenberg, Leopold, and Sklaroff [156] find that variation in concentration in the normal eye may run as high as 28%. Active inflammatory lesions may show a significant concentration of the phosphorus. Snodgrass, Lenihan, and Primrose [157] performed similar studies on four cases of malignant melanoma but found no appreciable difference in the phosphorus uptake between healthy and diseased eyes. However, Dunphy, Dreisler, Cadigan, and Sweet [158] agree with Thomas, Eisenberg, and their co-workers that radioactive phosphorus

† References 153 and 154.

is a useful diagnostic aid in dealing with intraocular tumors. Mullen, DeLong, and Steinmetz [159] obtained positive results when performing phosphorus uptake studies on a patient with metastatic carcinoma to the choroid.

MISCELLANEOUS CONDITIONS

Stefek [160] describes a patient in whom iridocyclitis developed four weeks after injury by lightning and subsided in two weeks. Minor subcapsular opacities of the lens developed into typical electrical cataract six weeks later. The iridocyclitis was thought to be due to minor necroses in the iris and ciliary body as a result of the lightning.

A review of the condition ophthalmia nodosa is given by Dreyer,[161] who reports a case in which caterpillar hairs migrated through the cornea and produced a nodule in the iris and chronic uveitis.

Paralytic mydriasis following herpes zoster ophthalmicus and subarachnoid hemorrhage is described in a case by Spota and Brage,[162] who believe that the ciliary ganglion had been involved in a virus infection.

The value of the Adler-Scheie test in the diagnosis of Adie's syndrome is emphasized in the report of three cases by Sprofkin. [163]

Reese and Blodi [164] describe the presence of extramedullary hematopoiesis in the histological sections of the eyes of 19 stillborn infants, 12 of whom were premature births. The blood-forming facilities were noted to occur primarily in the choroid. The authors suggest that the vitreous clouding occasionally seen in premature infants may be due to the presence of hematopoietic cells.

Cowper [165] gives an excellent detailed review of our present knowledge concerning angioid streaks and admits that the nature and origin of the condition is still unsettled. Cowper favors the theory that a weakness of the choroidal circulation with, at first, serous and, later, hemorrhagic extravasations, usually accompanied by migration of pigment epithelium to the affected vessels, seems best to account for the streaks, as well as the associated fundus pathology.

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Obituaries

HENRY MINSKY, M.D.
1895-1954

DR. HENRY MINSKY died suddenly of a cerebral hemorrhage on May 23, 1954, while visiting at Rhinebeck, N. Y. Dr. Minsky was born in New York on June 21, 1895, and spent his entire life in this city. He attended De Witt Clinton High School and Columbia College, obtaining his B.S. degree in 1917. In 1919 he was graduated from Columbia University College of Physicians and Surgeons and then interned for 18 months at Lebanon Hospital.

Dr. Minsky's ophthalmological training was as unique as it was thorough. A chance meeting with Dr. Oscar Diem shortly after entering medical school was to shape his entire career. Dr. Diem, a former assistant of Prof. Ernst Fuchs, found in Henry Minsky not only a receptive mind but also the rare spark that inspires the true teacher. During most of his medical school career the young student traveled every morning from Brooklyn to Woodlawn, arriving there at 6 a. m. for two hours of detailed instruction in ophthalmic fundamentals. At 8 a. m. he left to attend regular medical school classes. Shortly after his internship, he and Dr. Diem accompanied Professor Fuchs on a lecture tour of the United States, taking notes later published as "Notes and Remarks on Prof. Fuchs's Lectures."

Then followed several years of association before opening his own office, first with Dr. Diem, later with Dr. Charles H. May. Despite the very large practice he soon developed, he found time for much hospital work, research, and teaching. His first appointment was at the New York Eye and Ear Infirmary, where he became an assistant ophthalmic surgeon in 1921. In 1953 he was appointed to the consulting staff of this hospital. In 1924 he started as a clinical assistant at the Mount Sinai Hospital, rising through successive promotions to the position of ophthalmic surgeon in 1947. In 1934 he was appointed visiting ophthalmologist to the Harlem Hospital, serving in this capacity till 1951, when he became consulting ophthalmologist. He also served as consultant ophthalmologist to Hillside Hospital, Norwalk General Hospital, and Maimonides Hospital, in Liberty, N. Y. In 1947 he was appointed Associate Clinical Professor of Ophthalmology at Columbia University.

He was a Fellow of the American College of Surgeons, the New York Academy of Medicine, the American Academy of Ophthalmology and Otolaryngology, and the American Medical Association. He was a member of the New York Society for Clinical Ophthalmology, the Brooklyn Ophthalmological Society, the Pan-American Medical Association, and the New York Plastic Surgery Society, as well as a past president of the Metropolitan Medical Society.

His investigative interests were wide. Early contributions, born of his passion for careful and systemic examination, included an ingenious method of recording objective findings by means of consecutive diagrams, now widely known as "Minsky's circles." Later, his research turned to a detailed study of the anatomy of the zonule in relation to the pathogenesis of glaucoma and retinal detachment. His method of surgical repair of recent lid lacerations, a masterpiece of simplicity

and ingenuity, is universally recognized. His last contribution, published posthumously, concerning the "Correlation of Ocular Changes in Essential Hypertension with Diastolic Blood Pressure," culminated 20 years of careful observation, introducing many new and valuable diagnostic criteria.

He was a born teacher, whose first love was personal instruction, both at the bedside and at the operating table. Realizing the need, however, for more formal courses, he expanded the Mount Sinai Hospital's teaching program, organizing several symposia tailored primarily to the needs of ophthalmologists returning from military service, in addition to a complete roster of individual courses. Through these courses, as well as the aid and the encouragement offered for research, his staff enjoyed unusual opportunities to develop themselves in special fields. Nothing gave him more pleasure than to see recognition accorded those whom he had trained and sponsored.

To him a patient was not just an ophthalmic problem, but a complex human being who, both physically and psychologically, required complete and unhurried study, as well as kindness and consideration. This same warm approach won him an enormous circle of friends, to whom he gave of himself in many ways.

Despite the taxing demands upon him, he found time to engage in a number of relaxing pursuits, of which painting and etching, in which he excelled, were his favorites. An accomplished musician, he composed several works for piano and small instruments. Other hobbies included his stamp collection, photography, and gardening. His greatest happiness, however, stemmed from his own family associations. His home was a happy oasis where all the friends of every member of the family were always welcome.

On June 4, 1922, he married Fanny Judith Reiser, who survives him, as do his children, Charlotte, Marvin, and Ruth, several sisters and a brother, Dr. Arthur Minsky, an ophthalmologist.

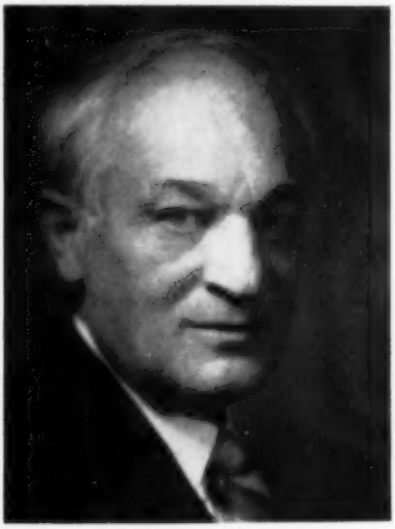
For all those who knew Henry Minsky, his passing has meant a deep personal loss, one that will long be felt.

Frederick H. Theodore, M.D.
Joseph Laval, M.D.

MARTIN COHEN, M.D.
1870-1954

Dr. Martin Cohen, who was active in ophthalmological research and teaching for half a century, died in New York on Oct. 29, 1954, at the age of 84.

Dr. Cohen graduated from the College of Physicians and Surgeons in 1898 and interned at the Hebrew Orphan Asylum Hospital. He began his ophthalmological studies in Vienna. From 1905 to 1920 he was on the staff of the Ophthalmic and Oral Institute at 13th Street and Broadway, which institution later became



MARTIN COHEN, M.D.
1870-1954

the Knapp Memorial Hospital. In 1915 he was appointed Director of Ophthalmology of the New York Postgraduate Medical School and Hospital. Until 1939 the hospital served as his center for activity in research and teaching. Hundreds of ophthalmologists started their basic training in Dr. Cohen's popular lecture halls at Postgraduate (now University) Hospital on East 20th Street.

He was an enthusiastic investigator and the author of eighty papers, published between 1903 and 1952. The general trend of his studies can be divided into three groups:

1. Research. From 1911 to 1918 he worked with Dr. Hideyo Noguchi in the study of trachoma at the Rockefeller Institute. Later Dr. Cohen became interested in the chemistry of the humors of the eye and their comparison with like components of the blood and spinal fluid. He devised a mercury tonometer, a fundus colorimeter, and a device for examination of distant stereoscopic vision for form and colors.

2. Reports of unusual clinical cases. Among these one may mention "Binocular Papilledema in a Case of Torulosis Associated with Hodgkin's Disease" (1945), and "Essential Shrinkage of the Conjunctiva in a Case of Epidermolysis Bullosa Dystrophica" (1935) as illustrative of this series.

3. Eye expressions of systemic disease. Subjects considered in this group were the value of eye findings in patients with fractured skull and eye manifestations of blood dyscrasias, diabetes, cardiovascular renal disease, and syphilis. In 1946, he wrote on ophthalmological findings in essential hypertension as a guide to sympathectomy.

From 1918 to 1919 he was chairman of the Section on Ophthalmology of the New York Academy of Medicine. In 1923 he was honored as the first New York ophthalmologist to receive the Knapp Memorial Medal, for his paper "Significance of Pathological Changes in Fundus in General Arterial and Kidney Disease."

He was a member of the American Ophthalmological Society, the Society of Experimental Biology and Medicine, the New York Academy of Medicine, and the New York Society for Clinical Ophthalmology.

In recent years he was a consultant at University Hospital, Manhattan Eye, Ear and Throat Hospital, Hospital for Joint Diseases, and Harlem Hospital.

Despite the pressure of his ophthalmological work, he found time as a good citizen to be honorary eye surgeon for many years to the New York Police Department, vice-chairman of the Selective Service Medical Advisory Board, and president of the Board of Visitors at the Manhattan State Hospital.

Dr. Cohen brought to his research wide scholarship and originality. His profound knowledge was manifested with extreme modesty. His personal relations were characterized by gentleness and kindness; his friendship was given with loyalty and generosity.

His extraordinary love and devotion as a teacher and in research inspired many of our present-day leaders in ophthalmology.

He is survived by his wife, Eugenia Adler, and his son, Peter.

JAMES W. SMITH, M.D.

Books

Transactions of the Pacific Coast Oto-Ophthalmological Society, Vol. XXXV. Morrissey Bros., Los Angeles, 1954.

The 38th Annual Meeting of the Pacific Coast Oto-Ophthalmological Society was held at the Royal Hawaiian Hotel in Honolulu, Hawaii, from Monday, April 26, to Thursday, April 29, 1954. The president, Dr. Leland Hunnicutt, of Pasadena, Calif., presided. Dr. A. Ray Irvine Sr. was the guest of honor. The following ophthalmological papers were presented:

President's Address: Role of Experimental Work in Our Specialty	Leland Hunnicutt
Eye, Ear, Nose, and Throat Injuries Sustained in the Korean Theater	Col. Austin Lowrey Col. Frank Shaffer
Changing Concepts of Ocular Leprosy	William J. Holmes
Ocular Findings in Disseminated Lupus Erythematosus	Thomas W. Cowan
Cobra Venom in Ocular Therapy	L. Weston Oaks James H. Quinn
Removing the Backache from Cataract Surgery	Philip M. Corboy
Visual Disturbances Following Acute Blood Loss	Joseph E. Alfano Kenneth L. Roper
Reconstructive Surgery of the Lids and Conjunctiva	Merrill J. Reeh Charles W. Browning
Late Results of Penetrating Keratoplasty	Max Fine
Leprosy of the Eye, Ear, Nose and Throat	Forrest J. Pinkerton

The *Transactions* for this meeting supply the papers in full, together with many other papers of greater interest to otolaryngology, and with the discussions and the proceedings of the meetings.

The 39th Annual Meeting will be held in Portland, Ore.

Refraction and Body-Growth. By G. S. Pendse, Ophthalmic Surgeon, Poona, India. Pp. 94, with 29 tables, and 9 graphs, and 1 photographic plate. Indian Medical Research Memoirs, No. 38. The Indian Council of Medical Research, New Delhi, 1954.

This monograph contains many literary gems of research from Claude Bernard and others, discussions of elementary statistical methods, and some data on myopia. The history of studies on myopia is briefly reviewed. It is agreed that myopia of less than —3.00 D. is merely a statistical variation of hereditary factors, such as corneal curvature, lens power, and axial length of the globe. Myopia of more than —6.00 D. should be considered separately because of a high incidence of degenerative changes.

There will be conflict with Pendse from those who believe that the rate of increase of myopia in children is to any degree affected by nutrition, near work, posture, and convergence. Pendse measured the myopia under atropine cycloplegia of the following children: 590 Brahmins, 618 Chitpavans, and 645 Untouchables. The genetic lines are certainly different. The first two groups are well schooled, and the last group receives no schooling; yet there is more than twice the incidence of myopia in the Untouchables. Pendse uses this evidence to disprove the school work theory of myopia but does not enlarge on the dietary difference

in the two castes. The frequency distribution curves for ametropia departed from normal with a *t* of 6.58 in Brahmins, 5.47 in Chitpavans, but 11.04 in the Untouchables.

Pendse reported a small series of myopic children and controls on whom determinations of hemoglobin and serum calcium and phosphorus were made. He concluded that in the myopic children under the age of 12 years the findings were subnormal, but the difference was barely significant.

No data are presented on the incidence of exophoria or esophoria, fusion or suppression, anisometropia, asthenopia, or the like. No information about the treatment of the cases reported is given.

A part of the data from the monograph appeared in the September, 1954, issue of the ARCHIVES, page 404. Except at the age of 12, the degree of myopia found in children at various ages is equal in girls and boys. The slight excess of myopia found in the girls at the age of 12 was attributed to the endocrine changes and the spurt of growth present during the following year. In the monograph, these data are interpreted to correlate rate of growth in weight and height with the rate of change toward myopia. However, boys and girls are considerably different in their growth rates both before and after the age of 12, without corresponding differences in the degree of myopia. Before 12, the girls are larger but not more myopic. After 12, the boys grow rapidly larger, but, again, are not more myopic Pendse makes unwarranted conclusions from a relatively small number of cases.

Only 11 patients were followed over a period of time, and most of these for only two years. One case seemed to illustrate Pendse's thesis. A girl at the age of 9 years was —4.00 D. myopic and 50 in. (127 cm.) tall. The next two years, she gained 1.7 in. (4.3 cm.) per year, and her myopia increased —0.75 D. per year. Then menstruation started. In one year she gained 8 in. (20.3 cm.) in height and —2.50 D. in myopia. The second year, from ages 12 to 13, she gained only 1 in. (2.5 cm.) in height, and the myopia remained stationary at —6.50 D. Some of the other cases were less dramatic. One gained 4.5 in. (11.4 cm.) and —1.50 D. per year. Another gained 2 in. (5 cm.) and —0.50 D. per year.

A Stereoscopic Atlas of Human Anatomy. By David L. Bassett, M.D. Section I. The Central Nervous System: Reels 1-34. Section II. The Head and Neck: Reels 35-84. Sawyer's, Inc., Progress, Portland, Ore. 1954.

The publication of these two sections of this Atlas, which presents in stereoscopic colored photographs the dissected structures of the human body, is a boon to the teaching of ocular anatomy. It will repay any ophthalmologist who is teaching or in the process of learning, or, for that matter, just reviewing anatomy for the love of it, to invest in these beautiful pictures.

Each Section comes as a series of small books, each consisting of a series of line drawings made from the photographs of the actual dissections. In the back of each booklet are eight circular Viewmaster reels, each contained in a handy envelope. Each reel can easily be inserted in the Viewmaster stereoscope, sold with the books. This can be lighted by batteries or by connecting it with an electric cord to house current. On each reel there are seven views, each seen stereoscopically, of a particular dissection. Each line drawing has captions plainly marked by numbered lines, pointing out the details which that particular dissection demonstrates. The dissections made by Dr. Bassett, who is Associate Professor of Anatomy at Stanford University, Calif., are excellent, and the Kodachromes by William Gruber are superb. It is difficult at best to make close-up photographs of anatomical dissections, and these which are shown in three dimensions add immeasurably to the value of the "Atlas" as a teaching medium.

Section I deals with the central nervous system and depicts the coverings of the brain and cord and the actual dissection of the brain from every conceivable aspect. The cerebrum is dissected from above, below, laterally, medially, and in frontal sections. In a similar way, the cerebellum and the spinal cord are treated, and a special section gives roentgenograms of the brain. It is a remarkable feat, and one of the best visual aids to teaching which has yet appeared.

Section II deals with dissections of the head and neck. Of chief interest to ophthalmologists are the sections dealing with the eyelids, dissection of the left orbit from an anterior approach, dissection of the right orbit from a superior approach, dissection of the left orbit from a lateral approach, the orbital fascia, the apex of the orbit, the insertion of the extraocular muscles, and the dissection of the eyeball itself. Even if it is necessary to purchase the other views which do not directly relate to the eye and its adnexa, this section is well worth it.

Maxillofacial Anatomy—with Practical Applications. By Harry H. Shapiro, D.M.D. Price, $12.00. Pp. 392, with 314 illustrations, 46 in color. J. B. Lippincott Company, E. Washington Sq., Philadelphia 5, 1954.

While this book may have been primarily designed for students and practitioners of dentistry, it contains an excellent section on anatomy of the orbit and its contents for the practicing ophthalmologist. The author is, in fact, the attending maxillofacial surgeon in plastic surgery at the Manhattan Eye, Ear and Throat Hospital in New York. The illustrations are excellent. It will be useful to supplement the standard works on anatomy.

Neurosurgery of Infancy and Childhood. By Frank D. Ingraham, M.D., and Donald D. Matson, M.D. Price, $15.00. Pp. 456, with 482 illustrations. Charles C Thomas, Publisher, 301 E. Lawrence Ave., Springfield, Ill., 1954.

Ophthalmolgoists will find this a valuable book because of the frequency with which intracranial lesions first manifest themselves in ocular signs and symptoms. Strabismus, of sudden onset, is a frequent and early sign in the commonest form of intracranial tumor in childhood. Papilledema is notoriously a diagnostic sign in all space-taking lesions of the cranium.

Although considerable space, naturally, is taken up with operative techniques which do not primarily interest the ophthalmologist, plenty of space is devoted to ophthalmological subjects. The most valuable chapters are those on hydrocephalus, head trauma, and intracranial tumors. A separate chapter on tumors of the orbit emphasizes the transfrontal approach. The only serious error which could be found from an ophthalmological point of view was the failure to mention glaucoma in the chapter on the Sturge-Weber syndrome. This is unfortunate, since all those who deal with these cases should be reminded of the frequency of this complication.

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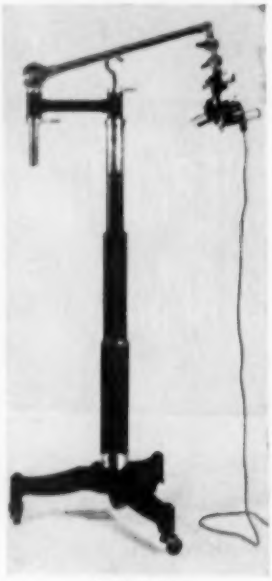

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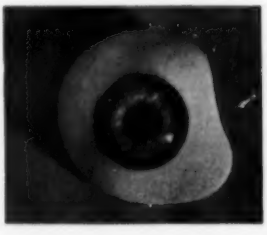

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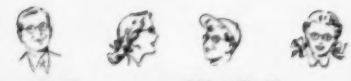

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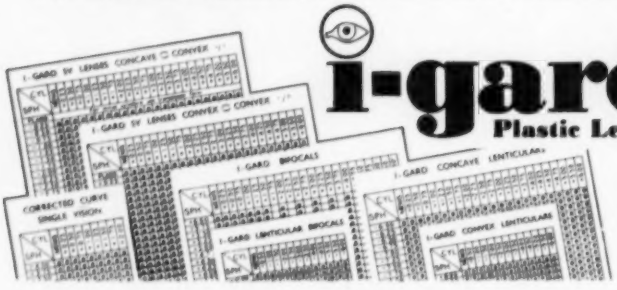

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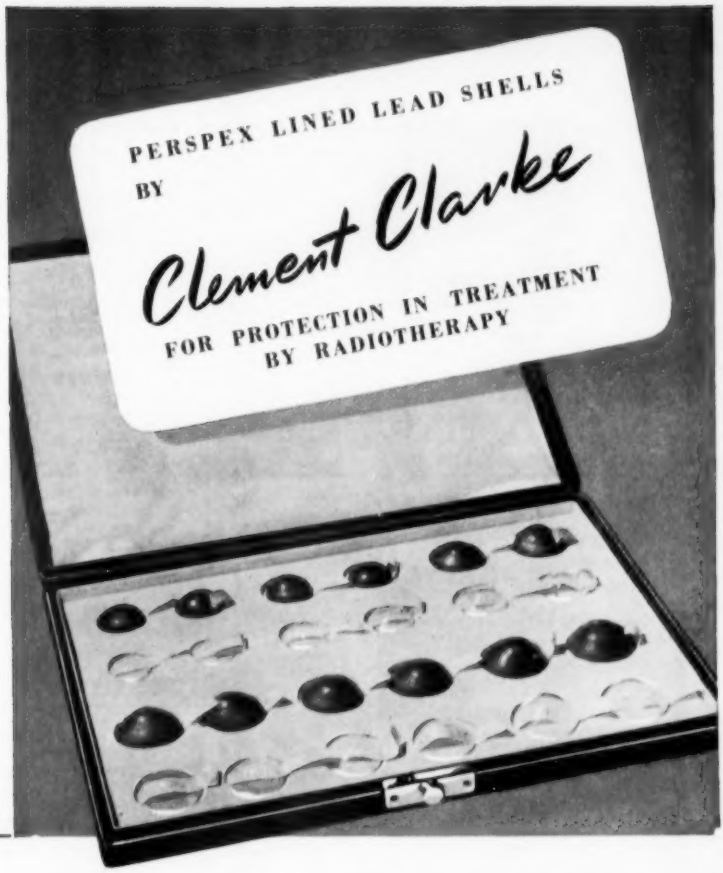

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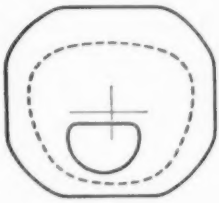

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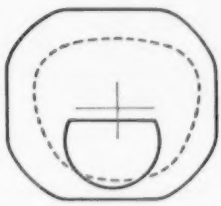

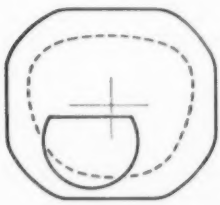

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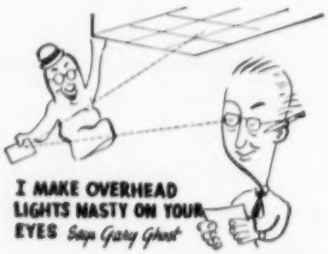

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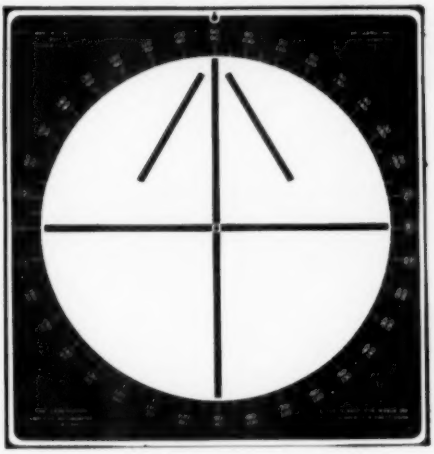

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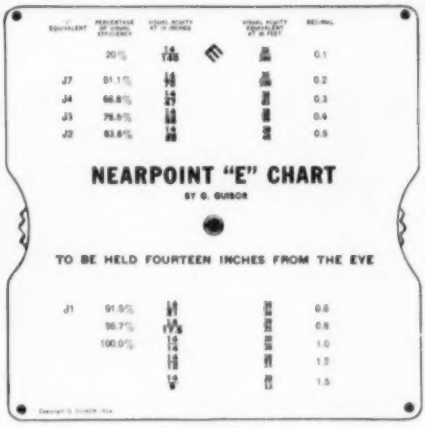

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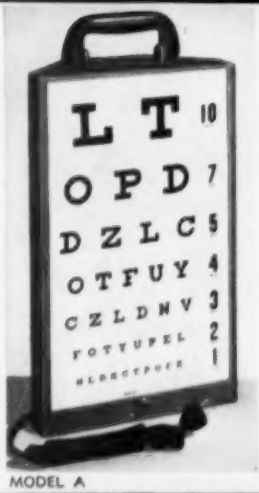

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